A.M.A.

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MARCH 1955
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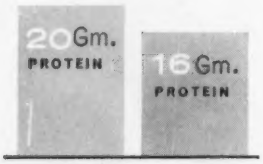

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1. Jeans, P. C., in A.M.A. Handbook of Nutrition, Philadelphia, Blakiston, 1951, pp. 275-298. 2. Stare, F. J., and Davidson, C. S., in The Proteins, American Medical Association, 1945.

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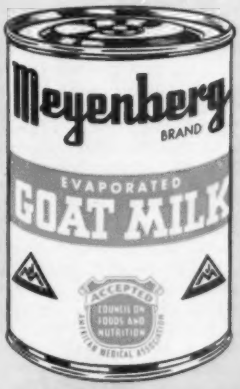

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Editorials

DR. CLIFFORD GROSSELLE GRULEE

THE RETIREMENT of Dr. Clifford G. Grulee in his thirty-second year as chief editor of the A. M. A. AMERICAN JOURNAL OF DISEASES OF CHILDREN comes almost simultaneously with his seventy-fifth birthday. He was born in Newport, Ky., on Jan. 3, 1880. A few years later the family settled in Oxford, Ohio, where he attended school and eventually graduated from Miami University, in 1899. He entered Northwestern University Medical School and graduated *cum laude,* in 1903. In 1901, as a result of studies in physiological chemistry carried on during summer vacations, he was granted the degree of M.A. by Miami University. In 1907 he married Margaret Freer, of Hinsdale. They have two children, Mary Freer Grulee (Capps), born March 26, 1908, and Dr. Clifford G. Grulee Jr., born June 9, 1912.

After a year of general practice he went to study in Vienna and Breslau under Professors Escherich and Czerny. Upon his return he became an associate in pediatrics at Northwestern University Medical School. In 1908 he became a member of the pediatric department at Rush Medical College, where he became the clinical professor and head of the department of pediatrics in 1924, a position he held continuously until 1941, when, upon the amalgamation of Rush Medical College and the University of Illinois College of Medicine, he became the Rush Professor of Pediatrics.

The year 1911 saw him a member of the board of directors of the Infant Welfare Society of Chicago, and he has continued to be active in the organization throughout the years.

His first book was published in 1911. This volume, titled "Infant Feeding," carried through four editions. His most recent contribution "The Child in Health And Disease," in which he was assisted by R. Cannon Eley, M.D., is now in its second edition. When the Central States Pediatric Society was formed, in 1911, he was one of the active founders' group. He served as secretary until 1921, and in 1922 was elected its president.

Following election to membership in The American Pediatric Society, he served as editor from 1924 to 1930. He became a member of the council in 1927, and was president of the council in 1934. In 1938 he was elected president of the Society.

When the American Academy of Pediatrics was organized, in 1930, he was the unanimous choice for secretary, a position he held until 1951, when he was made honorary president.

As a part of his interest in pediatrics, he collected all the publications available, both modern and historical. This material finally outgrew his home, and suitable quarters were found at The John Crerar Library, in Chicago, where it is known as the Clifford G. Grulee Pediatric Collection. Throughout the world it is recognized as one of the most complete pediatric collections in existence.

Innumerable honors have been bestowed upon him. He is a member of Beta Theta Pi, Phi Rho Sigma, Alpha Omega Alpha, Phi Beta Kappa, and Sigma Xi fraternities. He is an honorary member of the national pediatric societies of Bolivia, Peru, Mexico, Cuba, Uruguay, Brazil, Ecuador, Venezuela, and Colombia, and has received official decorations from the Cuban and Mexican governments. He was elected chairman of the American Committee for the Second International Congress of Pediatrics at Stockholm in 1930. In August of that year he was elected vice-president of the Congress.

DR. CLIFFORD GROSSELLE GRULEE

Clifford Grosselle Grulee grew up with pediatrics in the United States of America. As a practitioner, as a teacher, as officer of the Central States Pediatric Society, the American Academy of Pediatrics, and The American Pediatric Society, as author of Pediatric Texts and Articles, and as editor of the A. M. A. AMERICAN JOURNAL OF DISEASES OF CHILDREN, he has contributed to the development of pediatrics in a manner equalled by few.

We of the editorial board are deeply grateful for the opportunity of serving him.

DR. ROBERT BARRETT LAWSON

DR. ROBERT BARRETT LAWSON was born in Oakland, Calif., Aug. 21, 1911. At the age of a year and a half, his family moved to Foxboro, Mass., where he had his early schooling, following which he graduated from Harvard College, in 1932, and from Harvard Medical School, in 1936. He spent one year of general internship at the Rochester (N. Y.) General Hospital, and then went to Johns Hopkins Hospital, where he was a house officer at the Harriet Lane Home from 1937 to 1938. In 1938 he went to the Strong Memorial Hospital, where he

DR. ROBERT BARRETT LAWSON

was an assistant resident on the pediatric service, then spent another year as resident in the outpatient department. After finishing his residency, Dr. Lawson went to North Carolina to help with the organization of the pediatric department of the newly enlarged medical school, the Bowman Gray School of Medicine of Wake Forest College. During the first year of this organization, he held the position of pediatric consultant to the North Carolina State Board of Health, while he developed postgraduate courses for general practitioners in the field of child care. In connection with this teaching program, he held the position of professor of pediatrics at the School of Public Health of the University of North Carolina and the position

of associate in pediatrics at Duke University School of Medicine during the years 1940-1942. With the opening of the clinical teaching at Bowman Gray, he moved to Winston-Salem, N. C., in 1942, where he was successively assistant professor of pediatrics, associate professor of pediatrics, and in 1950 became professor of pediatrics and director of the pediatric department. In 1945, he was a fellow in the medical sciences of the National Research Council, spending a year in research in virology at the University of California and at Yale University. In 1954, Dr. Lawson moved to Miami, Fla., to head the department of pediatrics in the new University of Miami School of Medicine.

Dr. Lawson is a member of the Society for Pediatric Research, The American Pediatric Society, the American Academy of Pediatrics, and the American Medical Association. He is a member of the American Board of Pediatrics. He joined the editorial board of the A. M. A. AMERICAN JOURNAL OF DISEASES OF CHILDREN in 1950.

Epidermoid Carcinoma of Tongue and Floor of the Mouth in Infancy and Childhood

Report of a Case and Review of the Literature

FREDERICK W. MERRIFIELD, M.D., D.D.S.
WALTER WILLIAM DALITSCH, M.D., D.D.S.
and
MATTHEW M. STEINER, M.D., Chicago

Because the occurrence of epidermoid carcinoma in the floor of the mouth in a young child is unusual, it would seem appropriate to record the history of such a case, with a review of the pertinent literature. It would also seem in order to emphasize that, although this type of cancer and this location are infrequent in infancy and childhood, the condition must be always kept in mind and must be given due consideration in the differential diagnosis of any unusual and atypical lesions, regardless of the age of the patients.

Williams [1] stated that the incidence of cancer in childhood is low and that it is rarely seen in general practice. In special cancer hospitals he found only 181 cases. In graphs of the age incidence of his series, the peak occurrence of cancer in the childhood period was at 4 years of age. This was the age of our patient at the onset of her ailment. In analyzing the statistics of his and other reports, he found that in the age group below 25 years, cancer of the lip and tongue was very unusual. He found only one case of cancer of the tongue in the age group 15 to 25 years and no case below that age.

There appears, however, to be an increasing incidence of childhood cancer and also an increasing statistical mortality. Dargeon [2] has called attention to the high mortality rate of cancer in childhood. In certain childhood age groups, cancer (including leukemia and other tumors) has exceeded all other common diseases as a cause of death. This high mortality rate may be explained partly by a decline in deaths from other diseases. But there are also increasing recognition and more accurate diagnosis of neoplasms in childhood, which likewise produce an upward revision of the statistical incidence.

The wider recognition of this high mortality from cancer in childhood should stress the need for greater effort toward the establishment of early diagnosis of neoplasm in this age period.

Increased vigilance in the preschool group may bring many children under observation in time to effect a cure.

In a further analysis of the incidence of cancer, Dargeon [3] states that cancer of the breasts, uterus, and ovaries in the female, and cancer of the stomach, intestines, and prostate in the male, which comprise such a large proportion of the neoplasms in the adult, are so infrequent in childhood as to be curiosities. On the other hand, most of the types of tumors which are found in children seldom occur after maturity, although they have been described in the adult.

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Only by early diagnosis can the unfavorable prognosis of childhood cancer be altered. Some tumors, such as meningioblastomas and lymphomas, have a consistently poor prognosis. But with other varieties of cancer there is encouragement in reliable reports of long periods of survival. There is an increasing number of survivals 5 to 10 years after treatment. It is often supposed by parents that cancer is always fatal in a child, but this hopeless attitude is not justified. The important age group in which a reduction of the death toll may be realized is from birth to 5 years of age. The largest number of deaths from cancer occur in this period, but there is also a larger number of curable types of cancer.

Studies of a large series of sites of cancer in children indicate that there are six areas most frequently affected, in the following order: (1) bone, (2) kidney, (3) eye, (4) lymphatic and blood-forming organs, (5) soft somatic tissue, (6) nervous system. It is to be noted that carcinoma of the tongue and floor of the mouth is not mentioned, a circumstance which emphasizes its infrequency.

Tumors in infancy and childhood may arise in any subcutaneous structure. They appear usually as painless silent swellings and in many cases are considered to be hematomas. With few exceptions, any nontraumatic swelling should suggest cancer; any traumatic swelling that does not regress in the usual time and manner should be considered to be cancer unless clinical characteristics, or, preferably, biopsy, prove otherwise. Operative removal is the recommended treatment.

Helmholz,[4] discussing malignant neoplasms in childhood, also emphasized that malignant neoplasms in childhood have an unusually high mortality. Sarcoma accounts for 97% of tumors in children, whereas in adults, practically 90% of afflicted persons have carcinoma.

The average age of carcinomatous neoplasms in Helmholz' patients was more than 10 years. Thus it is seen that only in the third five-year age period of childhood did carcinoma occur, and then only rarely.

Helmholz concluded that the early recognition of malignancy in childhood should be emphasized if the unusually high mortality is to be reduced.

Thus far we have noted some interesting general aspects of cancer in infancy and childhood. We should now consider the more specific topic of cancer of the tongue and floor of the mouth in young subjects. In a discussion of this topic, Saleeby [5] stated that carcinoma of the tongue in young people is rare. Of 11 leading radiologists he consulted, none had even observed a case, and up to 20 years of age, only eight cases of carcinoma of the tongue were on record.

Saleeby reported his own case of a 15-year-old girl. She had a lesion for two months on the left side of her tongue which was ulcerating and was about 1.5 cc. in diameter. Biopsy showed a squamous-cell epidermoid carcinoma with pearls of keratinization. Radiation therapy produced a local recession. Enlarged lymph nodes on the right side of the neck, that is, on the side opposite the lesion, soon developed. More radiation therapy was given, but the response was poor, and finally cachexia and exitus occurred approximately one year after onset. A noteworthy feature of his case was that the first metastases were on the opposite side from the original lesion, which was interpreted as indicating a very high degree of malignancy. He tabulated 10 cases, his own making 11, of carcinoma in patients under 20 years. Special points that were common in these cases were as follows: neither mechanical irritation nor defective teeth could be blamed for the possible production of the cancer, no precancerous leucoplakia or syphilis was present, no tobacco-smoking or chewing habits existed as possible etiological factors, and there was no family background of carcinoma or hereditary syphilis.

The absence of these common predisposing influences inclines one to the conclusion that embryological and developmental factors must be seriously evaluated in a consideration of the genesis of these carcinomas.

There are some distinctive peculiarities of cancer of the oral mucous membrane that are worthy of emphasis, especially as pertains to duration, prognosis, and genesis. According to Geschickter's [7] observations, the durations of the symptoms of cancer of the tongue averaged less than cancer elsewhere on the oral mucous membrane. Ninety per cent of his patients gave a history in terms of weeks, whereas cancer elsewhere would give a history of months. The white patch, nodule, or ulceration on the tongue is readily seen and palpated, and so diagnosis should be possible early. Pain, bleeding, and fixation of the tongue are common features.

Regaud [8] was of the opinion that in cancer of the tongue palpable lymph nodes are much more likely to be invaded by metastases of the tumor than in cancer of the lip.

An interesting discussion of the embryogenesis of cancer is presented by Geschickter. He reviews the embryological development of the tongue, lip, and gum (after Hiss). The lower lip and lower gum and the buccal aspect of the tongue are derived from the mandibular arch or the first branchial arch. The pharyngeal area of the tongue is derived from the hyoid arch, or second branchial arch. About the fifth week the right and left lingual buds arise and bury the median bud, which is designated as the "tuberculum impar." Then about the seventh week the two portions of the tongue fuse with the alveolar and labial ridges of the mandibular arch. Epithelial covering derived from the mandibular arch is in part from the ectoderm of the primitive stomodeum and in part from entoderm of the primitive pharynx.

Ninety per cent of cancers of the oral mucous membrance affect the epithelial covering which is derived from the mandibular arch; this includes the lower lip, the lower gum, and the buccal portion of the cheek in regions of the lower molars. This arch is the only branchial arch lined by both entoderm and ectoderm. Carcinoma of the lip appeared to be frequent at sites of juncture of skin and mucous membrane. Carcinoma of the tongue seemed most frequent at sites of fusion of the ectoderm and entoderm. Such is the region where the pharyngeal area of the tongue, which is derived from the hyoid arch, and the buccal area of the tongue, which is derived from the mandibular arch, are fused in the process of embryonic development.

There are, apparently, clinical differences in tumors arising upon sites of different embryological origin. Considering that the mucosa of the anterior two-thirds of the side of the tongue derives from the lingual projections (tubercula lateralia) of first branchial arch and is of ectodermal origin, Ward and Hendrick [9] have concluded that tumors from this area are more differentiated, tending to the development of squamous-cell carcinoma. They also are less radiosensitive but are more accessible to surgery and radiation therapy. This is to be contrasted with tumors that involve the mucosa of the root and posterior third of the tongue, which is derived from the entodermal anlage of the second branchial arch. These are more anaplastic, metastasize more rapidly, and are more sensitive to x-ray. Such embryological factors must be considered as quite significant in studying the possible etiology of cancer in young persons.

We shall now examine some further aspects of cancer of the tongue as to incidence and offer suggestions for its control. Ward and Hendrick [9] state that 1115 persons died of cancer of the tongue in the United States in 1938. No patient was under 20 years of age, a circumstance emphasizing the rareness of our case.

The commonest site was on the side of the tongue, the next on the base or posterior one-third, and then the anterior one-third. The least common was the under surface of the tip.

As to prognosis, if the symptoms were less than two months' duration, 66% of the patients were alive after five years. If the symptoms had persisted for two months to one year prior to diagnosis, only 16.6% were alive after five years.

The prognosis also varied considerably according to the size of the lesion. In a first group, where the primary lesion was less

than 1.5 cm. in diameter, comprising 11.1% of all cases, the five-year cure was 55.5%. In a second group, the primary growth was less than 3 cm.; these cases accounted for 17.3% of the total, and the five-year cure was 50%. Group 3, of indeterminate size with unilateral but operable cervical nodes, was 37%. Of these, 22% lived five years after treatment. Group 4, with invasion of surrounding structures and inoperable metastases, comprised 34.6% of the total, and only 3.6% were alive after five years.

These authors advised, on the basis of their experience, that radiation be given to every local regional node four to six weeks prior to radical neck section and that then a complete dissection en masse be attempted similar to that advocated by Halstead for radical breast amputation.

The location of oral cancer has an important bearing on the prognosis. While squamous-cell epithelioma of the anterior two-thirds of the tongue is twice as frequent as at the base, the five-year survival of cancer of the anterior two-thirds is 41%, as compared with a survival rate of only 22% for cancer of the base of the tongue.[10] Likewise, cancer of the floor of the mouth has a relatively poor outlook for five-year survival—21%.

Knowledge of the histological structure of cancer and its anatomical extent is essential before starting surgical treatment. Until such data have been obtained, neither radiotherapy nor combined treatment should be instituted. A large tumor in children is usually in a high state of malignancy. The parent tissue is a rapidly growing and developing tissue.

Many tumors are biologically inoperable even if surgical removal is feasible anatomically. Surgery and radiation are our main agents for treatment. In children, the effects of radiation, dosages, tolerance, action on tissue and on glands, and the effect on growth and calcification are all aspects of importance in this early age group.

During infancy and childhood, certain types of malignancy are found which are extremely rare in adult life.[11] They are histogenically of an embryonic nature. Examples are adenocarcinoma of the kidney, retinoblastoma, and neurocytoma. Occasionally, the cells which carry the defect may remain dormant for many years before they are stimulated to neoplastic growth. Then, some years after childhood, there is a phase of life which is practically free from neoplastic tumors. Ewing[12] stated that the decline in incidence during this period is of biologic importance because it suggests that the embryonal causative factors which were operative in infancy and childhood have exhausted themselves. For tumors occurring after these periods, new etiologic factors must be sought.

The need for collaboration in the study of tumors in childhood has been recognized by all those engaged in this field.[2] The satisfactory prevention and control of cancer, as of any disease, requires active measures, if available, for a progressive therapeutic attack before the disease has progressed to a period of doubtful cure.

The success of treatment is determined not alone by the capabilities of the surgeon and of radiotherapy, but also by the rapidity with which these measures are used to institute treatment for a potentially curable neoplasm. The outcome in an early case depends on how soon it is recognized and how promptly treatment is started. The current necessity is for early diagnosis. No member of the entire group of physicians concerned with the early detection of cancer—neither the surgeon, nor the radiologist, the pediatrician, nor the health officer—is now more important than the family physician, who usually sees the patient first and whose opinion and recommendations are the basis for the family's decision.

There are only a few cases reported in the literature of carcinoma in the floor of the mouth in very young children. One reference of carcinoma of the tongue in an infant 10 months old was reported by de Noronha.[13] His article reviewed various reports of carcinoma of the tongue, but none of the pa-

tients were less than 20 years of age. His own case was that of an infant 10 months old who had a papillomatous growth under the tongue involving the lingual frenum. The child died in a short time despite considerable x-ray therapy, and the diagnosis was confirmed on autopsy.

Frank, Enfield, and Miller's case of carcinoma of the tongue in a newborn child seems most unique.[6] They reported a case of cancer of the tongue in a newborn infant who happened to be the son of a doctor. The child was full term, but would not nurse. On examination it was found that there was a swelling on the left side of the tongue about the size of a pea, thought to be a cyst. A biopsy was taken at 2 weeks of age. The growth was found to be a papillary squamous-cell carcinoma of the tongue. This tumor on the left side of the tongue occurred at the junction of the posterior and middle third. There was no infiltration in the floor of the mouth, no palpable nodes in the submental, submaxillary, or deep cervical areas, and the baby was healthy otherwise. The lesion was excised and cauterized with an electric cautery. Microscopic section was identical with the biopsy specimen, that is, a papillomatous squamous-cell carcinoma showing invasion of the underlying tissue and some abnormal mitosis. Follow-up x-ray therapy was used over the node-bearing areas of the left side of the neck. Two years later, examination revealed no evidence of recurrence. This case was reported because it was the only one of carcinoma of the tongue in a newborn infant ever recorded and the youngest to have received radiation for malignant disease.

REPORT OF CASES

The case we wish to report was that occurring in a baby girl of Italian parentage, who was admitted to the Children's Memorial Hospital because of a swelling under the mandible which had been present since October, 1951. The tumor was partly excised from the floor of the mouth in another hospital, and postoperative radiation had been given. However, the mass failed to resolve completely. Physical examination showed a somewhat pale child presenting a tumor of the left side of the tongue at the junction of the posterior and middle thirds. The more detailed history was that in October, 1951, when the child was still only 4 years old, the mother first noticed a swelling on the left side of the mandible, thought to be due to tooth infection. However, the teeth were examined and found to be normal. Five weeks later the patient was taken to a hospital, and a tumor was partially excised. The swelling receded somewhat, but did not disappear entirely. The patient received six x-ray treatments, with temporary relief. In the week before being taken to the Children's Memorial Hospital, the induration increased, and the patient had fever and complained of a pain in her back and legs.

The child's past history was not significant.

Family History.—Grandmother had a breast removed because of cancer. Grandfather "could have had bowel cancer"; no tuberculosis, diabetes, or allergy.

Physical examination revealed a well-developed well-nourished 5-year-old girl, not acutely ill.

There was a marked elevated induration on the left side of the tongue, and the child was unable to extend the tongue beyond the edge of the lip. The floor of the mouth was somewhat red and adherent to the tongue, and some yellow matter was present. On examination made by us, it was noted that the surface of the lesion was somewhat wrinkled and in folds. The appearance was characteristic of the macerated surface which is seen in mucous-membrane growths which have a hyperkeratinized surface kept moist by mucous secretions. This appearance resembled that of condylomata or similar granulating lesions on a moist surface. The margin of this lesion was irregular and not circumscribed or demarcated from the floor of the mouth or from the side of the tongue.

There was no bleeding, and the lesion was evidently neither painful nor tender to any great degree.

The pharynx was normal. Under the left mandible there was a fairly large firm induration, fixed to the skin and to underlying structures. This swelling was about the width of a hazelnut, extending from under the left mandible to the mentum. The tongue was indurated on the left side and was pushed up from the floor of the mouth and somewhat restricted in its motion. There was a slight regional adenopathy. The first impression was that the mass was a dermoid cyst.

On Jan. 30, 1952, surgery was performed on the left side of the floor of the mouth, and the firm induration was explored. Attempt was made to remove the friable mass of tissue from the lateral surface of the tongue and sublingual tissues. The tumor was of invasive quality, and it was difficult to identify particular structures. The lesion was seen to be much more extensive than anticipated and not of the traumatic or infected character at

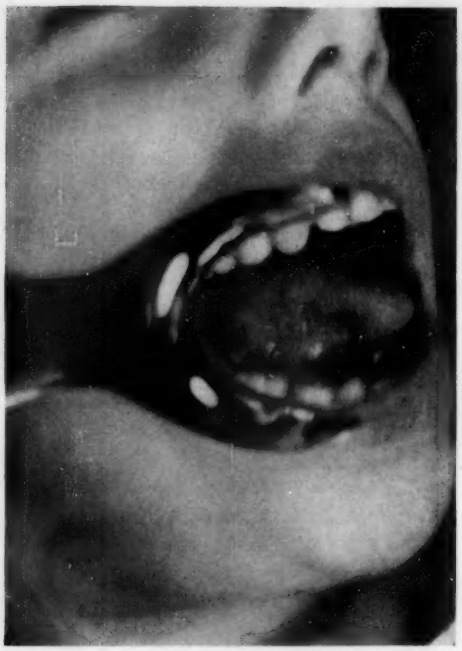

Fig. 1.—Epidermoid carcinoma on side of tongue in 4-year-old child. Lesion is indurated, adherent with irregular outline and surface.

first considered. This finding, together with the definite and extensive infiltrative character of the mass suggested malignancy. A large portion was excised and submitted for biopsy, but complete removal was quite impossible. The wound was closed as well as possible with mucosa, and the remainder was packed with iodoform gauze.

Pathological Report.—Specimens: Sublingual tissue, tissue from tongue, tissue from floor of the mouth, tissue from under the tongue; history of submandibular tumor.

Gross Description.—Specimen consists of several small pieces of tissue very irregular in size, largest measuring 2½×2×2 cm., all tissue corresponding to a submandibular tumor which was partially removed.

Gross Impression.—Deferred.

Microscopic Examination.—Sections of the tongue revealed the surface epithelium to be ulcerated and in some areas moderately hyperkeratotic. In all portions of the small quantity of surface epithelium at hand the epithelium was hyperplastic. In the submucosal tissue and extending deep into the skeletal muscle were nests of round elongated epithelial cells. In one area the cells could be seen to extend down from and to be continuous with the overlying stratified epithelium. Deep in the submucosal tissue, these cells formed nests and sheets. In certain areas, well-formed pearls were present. These nests of keratinizing cells are frequently found within endothelium-lined spaces. In all the material examined, which included material taken from deep into the tongue, similar neoplastic cells were seen. Mitotic figures were moderate in number. The cells were moderately well differentiated.

Diagnosis (No. 612-881).—Epidermoid cancer of the tongue.

X-ray examination of the skull and mandible showed no evidence of involvement. Further x-rays revealed no metastases.

The patient was seen subsequently on Feb. 6, 1952, a week after surgery, and two large submaxillary glands were noted, much increased in size since surgery. Two months later the patient had bilateral adenopathy; the cervical lymph nodes were large and uncomfortable. The metastases had crossed to the opposite side. On March 19, 1952, it was noted that the bilateral glandular metastases were rapidly increasing in size, causing considerable embarrassment to swallowing and breathing. The child did not eat well and was losing strength and weight. There were several episodes of hemorrhage which subsided when pressure was applied. A

Fig. 2.—Section showing strands and sheets of epithelial cells extending deep into submucosal and muscle tissue. Nests of keratinizing cells and pearls are present.

further observation, given in early May, reported that the patient was quite cachectic and rapidly losing strength and appeared to be nearing a terminal stage. Death followed soon after, about eight months after the onset and four months after the diagnosis was definitely established by biopsy section.

Summary.—An oral tumor occurring in a female child before her fifth birthday was first noted on the left side of the tongue, extending into the floor of the mouth. Early partial removal was performed. The tumor then progressed rather rapidly. Three months later complete surgical removal was attempted, but proved impossible. Biopsy established the diagnosis of epidermoid carcinoma of the tongue at the junction of the middle and posterior thirds on the left side, involving the floor of the mouth. It was noted that involvement of the regional cervical lymph nodes soon extended over to the opposite side. The patient was not benefited by surgery or x-ray. She rapidly progressed on a downhill course and died about eight months after onset and four months after biopsy confirmed diagnosis.

COMMENT

Several unique features in this case of childhood malignancy stand out. They are the early age of onset, the unusual character of the tumor (epidermoid carcinoma), and the infrequent site, i. e., the side of the tongue and the floor of the mouth.

The location of the tumor at approximately the junction of the middle and posterior third of the side of the tongue strongly points to an embryological cell rest as the possible etiological factor. The fact that other cases have occurred at this location suggests that it is a site of predilection on the basis of embryological development factors.

Cancer of the tongue has been emphasized as a severe form and of great malignancy because of the extreme vascularity and abundant lymphatic supply, permitting metastases to develop early. [14] In spite of the best management, the prognosis is often unfavorable.

That the lesion in our patient existed for several months before its malignant nature was suspected emphasizes that cancer should more often be considered in infancy and childhood; as Cowdry [15] puts it, "Children can have cancer too." Despite the rarity of epidermoid cancers in childhood as compared with those of mesodermal origin, the possibility of their occurrence must be kept in mind. Even though carcinoma of the tongue is most commonly an adult ailment, it cannot be ignored as a childhood lesion.

Review of the literature indicates that carcinoma in early childhood is relatively rare; that tumors of epithelial origin are quite rare; that cancer of the tongue in young people is very unusual, and that there are very few such cases reported under the age of 20 years. One was reported at the age of 15 years, one at the age of 10 months, and one at 2 weeks of age. Our case, starting at the age of 4 years, would seem to be the third youngest on record.

CONCLUSIONS

A case, probably the third youngest on record, is reported that illustrates many of the points discussed: a rapidly growing highly malignant type of epidermoid carcinoma of the tongue and floor of the mouth, beginning at the unusually early age of 4 years and having its probable origin in embryological cell rests which had become anaplastic and actively growing. The tumor had previously been treated as a cyst, but growth continued unchecked.

Cooperative study and observation by pediatrician, surgeon, radiologist, and pathologist resulted in the establishment of the true diagnosis. However, by that time, treatment by partial surgical excision and radiotherapy was of very little benefit and had no effect on the progress. Rapid spread to regional lymphatic nodes followed, and cachexia and death occurred soon after.

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The Use of Warm Blood for Exchange Transfusions

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INTRODUCTION

There are many factors which affect the condition of an infant during an exchange transfusion. To date little thought has been given to the possibility of the adverse effect which may be caused by the introduction of a large volume of cold blood into an infant's circulatory system. Regardless of the temperature of the blood in the reservoir, it approaches room temperature as it is given to the baby. This is due to the relatively small calibre of the tubing, which exposes a large surface of a small volume of blood to the ambient temperature. We have observed that the temperature of the blood at the point of introduction into the umbilical vein varies from 70 to 80 F. It is necessary for the infant to supply enough heat to raise the temperature of 500 cc. of blood 18 to 28 degrees.

Different methods of preventing the loss of body heat have been described in the literature. Our procedure is to restrain the infant on a circumcision board and then place him in an Armstrong incubator. With the incubator top open the air temperature is maintained at approximately 85 F. The infant is covered completely with surgical drapes except for the umbilicus. Oxygen is given to maintain a concentration of 65% about the infant's head. The exchange transfusion is started as soon as the indication for this operation is established, usually four to six hours after birth, the youngest infant being 1½ hours of age and the oldest, 64 hours. About 500 cc. of freshly drawn citrated blood is used.

It was noted that the rectal temperatures of the infants (21 cases) treated before the use of a blood warmer were 97 to 99 F at the beginning of the procedure and fell to 96 to 94 F at the end of the transfusion. Four of these babies, after approximately 250 cc. of blood had been exchanged, developed the appearance of being in shock. The blood withdrawn from the infants at this point had changed from the bright red color of oxygenated blood to the dark color of the blood being given, indicating that these infants had suddenly stopped oxygenation of their bloods. Two of the infants died at this point; in the remaining two cases the procedure was terminated, and the infants thereafter had an uneventful course.

In searching for some explanation of this "shock-like" condition, it was felt that the temperature of the blood might have been a major factor. It was decided to investigate the possibilities of warming the blood. There are a few questions to be answered. Will warming the blood increase the clotting difficulties to the extent of creating a hazard? Can the equipment be made simple and reliable enough so that its complexity will not introduce new hazards? Will warming the blood produce any chemical changes in the blood? And finally, will warm blood improve a baby's chance of survival?

DESCRIPTION OF APPARATUS

Two different blood-warming devices have been made. The first consists of a heat exchanger to warm the blood while it is flowing

From the General Electric Research Laboratory (Dr. Wilson).

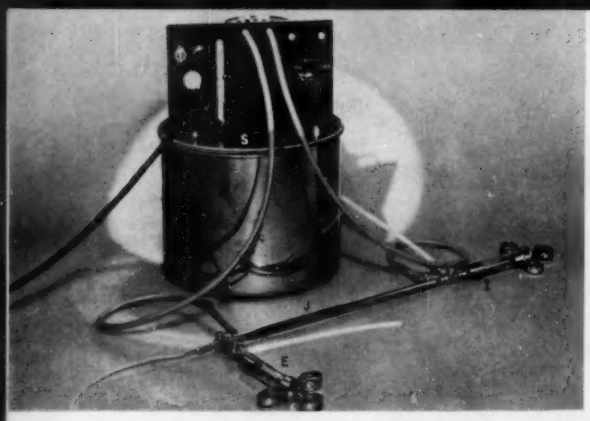

Fig. 1.—Blood warmer with metal heat exchanger, *J*. The equipment in the kettle thermostatically controls the temperature of the water bath and circulates the water through the heat exchanger.

from the syringe to the baby. This equipment is shown in Fig. 1. The heat exchanger, *J*, consists of a stainless steel tube 12 in. (30.5 cm.) long and 3/100 in. (0.08 cm.) inside diameter, about which a water jacket has been placed. Warm water is pumped through the outer jacket. Syringe *I* is used to pump the blood through the inner tube and into the baby. Syringe *E* is used to draw the blood out of the baby. With the circulating water at 103 F and the blood being introduced at 10 cc. per minute, the baby receives the blood at 99.5 ± 0.5 F. If two physicians are performing the operation, one can reload Syringe *I* while the other is extracting the baby's blood into Syringe *E*. This speeds up the operation, but probably a larger advantage of the double syringe assembly is that the baby's blood which is susceptible to clotting does not have to be drawn through the heat exchanger. The thought is that the clotting process is a chemical reaction that may be accelerated by the higher temperature in the heat exchanger. In addition, all the metal and glass parts have been coated with General Electric silicones to reduce the clotting. Essentially no clotting difficulties have been encountered using this equipment.

Fig. 2.—Blood warmer using glass helix, *A*, which is immersed in a temperature-controlled water bath.

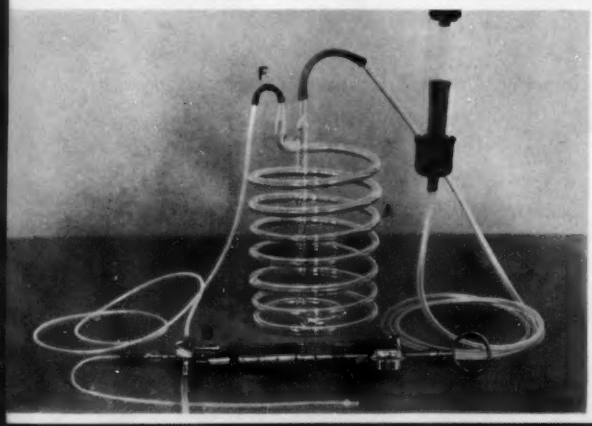

Figure 1 also shows the thermostatically controlled water bath from which the water is pumped to the heat exchanger.

Figure 2 shows a second device, developed more recently, which warms the blood before it enters the syringe. During the time that 20 cc. is being exchanged, the 20 cc. for the next cycle is being warmed in a helical pyrex glass tube, *A*, that is placed in the water bath at *S* of Fig. 1. A special small-heat-capacity four-way stopcock, *B*, facilitates the manipulation and reduces the cooling of the blood after it has been preheated. With this equipment the temperature of the blood that the baby receives may vary from 96 to 100 F. Probably this control is sufficiently accurate, and, therefore, this second method may be preferable because of the ease of manipulation.

Under normal operation in both devices no part of the blood is heated above 103 F, and this temperature is maintained for only three minutes or less.

Quite often removal of blood from the baby using a standard polyethylene catheter is difficult. It appears as though the vein sucks against the end of the tube and closes the tube like a flap valve. A new polyethylene tube catheter with a special terminal guard has been developed which greatly facilitates the withdrawal of the blood from the baby. The guard merely consists of a spherical expansion of the tube near the end (*D*, Fig. 2). The tubing is perforated adjacent to the expansion.

COMMENT ON PRELIMINARY OBSERVATIONS

To date, the first device (Fig. 1) has been used on 17 cases. In these cases the rectal temperatures remained the same or rose one degree, except for one infant, whose temperature fell from 95 to 94 F during the operation. None of these infants exhibited signs of shock or failure to oxygenate its blood. In most cases the operation progressed so well that the entire 500 cc. of citrated blood was used. The clinical impression is that the

general well-being of a baby is better when the blood warmer is employed.

There is a possibility that other improvements in the techniques of performing the operation were introduced unknowingly so that even without the blood warmer the last 17 cases would have been uneventful. However, near the end of this series, owing to a temporary breakdown of the equipment, two operations were performed without the blood warmer. Both of these showed initial symptoms of shock. In these cases the exchanges were stopped at 250 cc. and 300 cc., and the babies' final temperatures were 94 and 95 F, respectively.

In a third case another physician had an infant under severe shock, and efforts to exchange cold blood did not improve matters. After injecting 5 cc. and then 15 cc. of warm blood, the baby recovered and improved markedly within a few seconds. In these operations an infant goes into or comes out of shock so rapidly one is led to believe that something more than just the body temperature is involved. It is interesting to note that without knowing of these observations Dr. Warren E. Wheeler, of Columbus, Ohio, wrote to one of us as follows:

> It occurred to us that the main effect of a stream of cool blood entering the baby through the catheter and probably directed against the auricle would be to produce cardiac arrhythmias.

To gain some information on this point one would need to monitor babies routinely with electrocardiograms. Babies receiving cold blood and those receiving warm blood could be montitored in the hopes of observing the reaction of the heart as a baby goes into shock. The writers are not aware of any observations of this kind.

The second technique, preheating the blood in a glass helix, has been used only four times. The special catheter and the four-way valve make this "plumbing" slightly more convenient to manipulate than conventional equipment which does not heat the blood. With silicone coatings on all metal and glass parts, no clotting difficulties are anticipated.

CONCLUSIONS

It seems to us too early to draw any definite conclusions; however, these initial observations cited above indicate that warming the blood does improve the apparent condition of the baby during the operation.

Equipment simple to manipulate has been made that will deliver the blood to the baby close to normal body temperature; will not heat the blood over 103 F, and usually holds the blood at this temperature for only a few minutes.

So far no new hazards or harmful reactions have been observed.

Distribution of Lead in Blood as Affected by Edathamil Calcium-Disodium

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The effectiveness of edathamil calcium-disodium (calcium disodium ethylenediamine tetraacetate [Ca EDTA]) in stimulating the excretion of lead * suggests that it must exert a profound influence upon the binding of lead to tissue sites.

The experiments to be reported were designed to determine whether a redistribution of lead from cells to extracellular fluid does occur during the therapy of lead poisoning.

EXPERIMENTAL DATA

Patients with history, physical examination, and bone x-ray changes suggestive of lead poisoning were treated with edathamil calcium-disodium subcutaneously, a single 1 gm. dose as a 1% solution in saline. Blood specimens were drawn and heparinized at intervals up to eight hours and separated into plasma and cells. Lead was determined on aliquots of blood and urine by a semimicro modification of the colorimetric diphenylthiocarbazone (Dithizone) method developed in this laboratory.[9] Five patients were studied, including three children and two adults. Data on the entire course of these cases will be reported elsewhere.

RESULTS

The Table shows the lead content of plasma and cells or whole blood of five patients who each received subcutaneously 1 gm. edathamil calcium-disodium at zero time, as a 1% or 2% solution in isotonic saline. Three of the five patients had blood lead concentrations considered to be within the normal range.[10] All, however, showed marked urinary excretion of lead in response to edathamil calcium-disodium. A decided shift in distribution of lead between plasma and cells can be seen in all cases by the second hour after administration of EDTA.

Plasma and Red Blood Cell or Whole Blood Concentration of Lead (Micrograms per 100 Ml.) After a One-Gram Dose of Edathamil Calcium-Disodium

Patient	Age	Tissue	Hours 0	2	4	8
Bo	3 yr.	RBC	275	186	68	34
		Plasma	63	123	80	55
Ep	Adult	RBC	15	...	23	3
		Plasma	2	...	17	19
B	Adult	Whole blood	61	...	70	100
		Plasma	0	...	27	48
R	4 yr.	RBC	12	...	109	..
		Plasma	0	...	139	..
AE	5 yr.	Whole blood	7	12	10	12
		Plasma	2	22	17	12

The plasma lead increased on therapy in all cases and appeared to reach a maximum in two of the five. Both of these cases had the highest plasma level at the second hour.

The Figure is a plot of the urine output of lead, micrograms per hour, urine volume in milliliters per hour, whole blood lead, and plasma lead of patient A. E., probably the most studied lead poisoning case in history; we have treated him three times, first in 1951. The urine flow and lead excretion at zero time are average values obtained from the total output of the previous 24 hours. It is apparent from these data that the plasma

From the Research Foundation of Children's Hospital.

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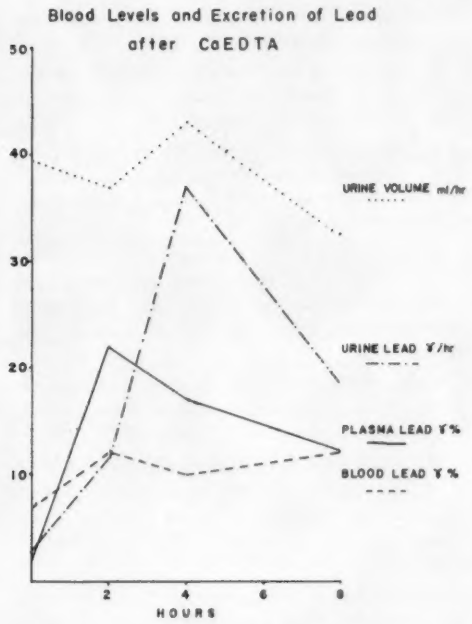
* References 1-3.



clearance of lead is at the rate of about 100 ml. per hour before treatment. After edathamil calcium-disodium it drops to about 50 ml. per hour at two hours, then to 230 and 150 ml. at four and six hours, respectively.

COMMENT

Edathamil calcium-disodium has been demonstrated to be highly effective in deleading humans and experimental animals. Although the chemical mechanism of chelation, by which edathamil calcium-disodium presumably affects the activity of lead ions in the organism, is well understood,[11] the physiological activity of this compound is still to be elucidated. Since edathamil calcium-disodium can equilibrate rapidly with almost all body fluids,[12] contact between the therapeutic agent and the toxic metal is reasonably assured. The rise in whole blood lead after administration of edathamil calcium-disodium [5] is ample proof, therefore, of a transfer of lead from tissue sites to the free fluid compartments. The evidence that the transfer is mainly to the plasma compartment of the blood as opposed to the red cell fluid is presented in this paper. Since the compound does not enter red cells,[12] these observations that red cell lead decreases during therapy, even to the point where the plasma levels are higher than the cell levels, suggest that the red cell lead is attached to sites at the cell surface accessible to edathamil calcium-disodium. The fact that the red cell level of lead drops even as the plasma level rises indicates a shift of lead from cells to plasma. The zero time data on all five patients are in agreement with previous observations that most of the blood lead is in the red cell fraction.[13]

The plasma clearance of lead is not changed remarkably by therapy, the amount excreted being roughly proportional to the blood level of lead, presenting the alternatives that the lead edathamil calcium-disodium chelate is mainly reabsorbed, or, more likely, is bound to protein. This is to be expected, since lead can form six coordinate bonds and at neutral pH edathamil calcium-disodium EDTA can occupy only four. The remaining two coordinate bonds could form a complex with a nondiffusible component of plasma.

The question of the binding of various solutes to plasma proteins is beyond the scope of this discussion, but it might be worth while to reemphasize the fact that altering the ionization of a metal or acid radical might not be as effective in removing it from protein as one might think. Mortensen found that the percentage of ultrafilterable lead in plasma increased from 6 to 30 when the citrate level was raised to 8 mg. per 100 cc.,[14] an amount far in excess of theoretical to chelate all the lead present.

In view of the rapid excretion of the calcium chelate,[12] the relatively slow clearance of the lead complex suggests that it is handled in a different manner by the kidney. This is in agreement with the finding of Maison [15] that, although edathamil calcium-disodium is not absorbed significantly from the gastrointestinal tract, lead edathamil calcium-disodium is absorbed very rapidly. The emunctory, as well as absorptive, metabolism of lead in the presence of a chelating agent

not only differs from the metabolism of the free cation but also appears to differ markedly from the metabolism of the chelating agent itself.

SUMMARY AND CONCLUSIONS

Five patients with lead poisoning were given edathamil calcium-disodium (disodium calcium ethylenediamine tetraacetate [Ca EDTA]), and the distribution of lead in plasma and red cells was determined at intervals.

Edathamil calcium-disodium causes an increase in plasma lead and a marked shift of the ratio plasma lead/cell lead to values greater than 1.

Although the plasma lead level rises many fold, the blood clearance of lead varies only about twofold. The marked stimulation of lead excretion seen with edathamil calcium-disodium is therefore due mainly to the increased plasma level.

It is suggested that edathamil calcium-disodium renal excretion of lead differs from that of edathamil calcium-disodium.

Dr. Ed Levy, of Norfolk, Va., and Dr. Jacob Brem, of Worcester, Mass., provided the specimens from three of their cases for this study. The edathamil calcium-disodium solutions were provided by the Riker Laboratories, Inc.

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Tetanus Immunization

XI. Study of the Duration of Primary Immunity and the Response to Late Stimulating Doses of Tetanus Toxoid

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Although the protective value of active immunization with tetanus toxoid has been conclusively established, there remains in the minds of many practitioners and responsible public health personnel doubt concerning the effectiveness of stimulating injections and the duration of primary immunity. There is especially confusion relating to the length of time a person may go following primary immunity and still develop a protective response to a stimulating dose of toxoid.

The following statements are generally accepted.

1. A blood serum level of 0.1 ATU/ml. is protective against the development of clinical tetanus.

2. A stated ATU level resulting from active immunization is far more effective protection than a corresponding level from passive immunization from the administration of antitoxin.[1]

3. Two or more doses (according to the manufacturers' specifications) of precipitated toxoid given at an interval of one to two months with a stimulating dose one year following the last dose of the primary series and every four years thereafter or immediately upon the occurrence of an injury affording the possible entry of Clostridium tetani will provide adequate protection against the development of clinical tetanus. This procedure represents the current immunization policy of the Armed Forces.[2]

4. The ATU level in the vast majority of cases rises well in excess of the accepted minimal protective level of 0.1 ATU/ml. within five to six days after a stimulating dose is given, when no more than four years have intervened after the last stimulating dose or the primary immunization.[3]

There is reason to believe that a protective level of tetanus antibodies persists far in excess of the currently accepted protective period.[4] Also, a prompt and adequate ATU response could be expected following a stimulating dose of appropriate toxoid at an interval far greater than the currently accepted four- or five-year period. There is some evidence that titers as low as 0.01 ATU/ml. may be highly protective in persons with a background of basic immunity.* However, information regarding this point is largely speculative, and there is no specific information available concerning the required levels in man.

Based on certain of the preceding considerations, this study was planned to further evaluate the following:

(*a*) The current immunity status (antibody levels) of persons who have had an approved series of tetanus toxoid at any time in the past.

(*b*) The antibody response among such persons to different doses and types of toxoid, with special reference to those having a historical interval of five or more years from the last stimulating dose.

(*c*) The collection of group data from which certain pediatric, industrial, and hospital routines might be considered or formulated in the prevention of clinical tetanus.

MATERIAL AND TECHNIQUES

The persons studied were employees of the Veterans Administration Hospital, Nashville, Tenn.,

Professor of Pediatrics, Marquette University School of Medicine (Dr. Peterson); Professor of Pediatrics, Vanderbilt University School of Medicine (Dr. Christie); Chief of Professional Services, Veterans Administration Hospital, and Associate Professor of Public Health and Preventive Medicine, Vanderbilt University School of Medicine (Dr. Williams).

* References 5 and 6.

who volunteered for the study. The group was composed entirely of veterans who had had service immediately preceding, during, or subsequent to World War 2. No effort was made to study the group according to the branch of service. The time interval in years was computed on the basis of the last-known stimulating dose. This time interval ranged from less than 1 year to as long as 13 years, with many who had not received an antigenic stimulus in 10 or 11 years. The group totaled 227 initially, including all types of employees, from the medical manager to day laborers. Of the 227 who started the study, a total of 219 are included in the final tabulations. Five are included only in persistence studies, and six are included only in response studies. Eight are not used in any tabulations, seven because inadequate serum samples were obtained and one because he turned out to be a nonimmunized World War veteran. Routinely a preliminary blood sample was drawn from each person and immediately following this he was given 0.25 or 0.5 ml. of fluid or precipitated toxoid. Second and third samples of blood were routinely drawn from each person on the 6th or 7th and the 13th or 14th days, respectively. The subjects were grouped according to place of employment and rotated in a manner which would provide a good distribution of types of toxoid and dosage among all groups of employees.

TABLE 1.—*Personnel of the Study*

Age, Yr.	Sex	Race		Total
		White	Negro	
<30	Male	37	20	57
>30	Male	89	53	142
<30	Female	0	0	0
>30	Female	20	0	20
Total		146	73	219

TABLE 2.—*Personnel and Materials by Groups*

Group	No.	Toxoid	Dose, Ml.
A	56	Fluid	0.25
B	55	Fluid	0.5
C	54	Adsorbed	0.25
D	54	Adsorbed	0.5
Total	219		

All blood specimens were given simple numerical identification as the subjects reported to the collection station. After clotting, the serum was aseptically separated and forwarded to Cutter Laboratories, where the antibody titrations were carried out. The tests were performed several weeks to months after the sera were collected.

The antibody titration technique was essentially the same as that approved by the National Institutes of Health, involving the use of standard toxin plus standard antitoxin. The standard N. I. H. tetanus toxin was used in all titrations.

The toxoids used in the study were regular commercial toxoids.†

The age, sex, and race of the study personnel are shown in Table 1. Except for a lack of white women in the younger age group and the absence of Negro women in both age groups, there was nothing unusual about the distributions.

The type and dose of toxoid given, the numbers in each group, and the groups are indicated in Table 2.

RESULTS

Of primary interest was the level of antitoxic immunity found in the group at the time of their booster injection and its relation to the time interval from the last antigenic stimulus. In order to secure reasonable-sized groups for comparison, the material was divided into four groups, those persons who had had immunization three years or less before, those who were immunized four to eight years before, those who had had nine or more years elapse from their last toxoid injection, and a fourth group where the interval was uncertain, a miscellaneous group. These observations are shown in Table 3. A simple inspection of this table indicates that the great majority of persons who have had previous immunization against tetanus had residual antitoxin levels which would probably be protective against tetanus infection. Only eight of the total group of 219 had titers below 0.01 ATU, and no person who had been immunized as recently as six years previously had a level that was lower than 0.1 unit. A conservative view would be to accept levels of 0.1 ATU as being protective and lower levels as being borderline. According to this perspective, it is apparent that all of those immunized within three years maintain protective levels of antitoxin. Actually none who had been immun-

† Toxoids from regular stock supplied by Cutter Laboratories, Lot D 4589 for fluid toxoid and Lot L 4201 for the adsorbed toxoid.

ized as recently as six years showed less than 0.1 units, but the number in the group four to six years is not great enough to draw any valid conclusions.

In the groups who had been immunized more than six years before testing, 50 of 162,‡ or 30%, showed ATU levels of less than 0.1 and would be considered to have only borderline protection, but only 8, or 5%, showed less than 0.01 ATU and might be critical risks against tetanus infection.

It is interesting at this point to inspect another variable which might influence the persistence of antitoxic immunity. For this purpose the group has been broken down into those who had only primary immunization and where discharge from the Army and other circumstances made it quite probable that this was the only antigenic experience they could have had. Second, a group who had had primary immunization plus one known booster immunization; third, a group who had had primary immunization and in addition had received multiple injections of toxoid for boosters, and fourth, a "miscellaneous" group who had had primary immunization and no record of booster injections but whose service connections were such that they may well have had secondary injections. Table 4 shows the persistence of antitoxic immunity in these groups. It is apparent that increasing experience with tetanus toxoid results in higher levels of sustained antitoxic immunity. However, it should be pointed out that this difference may be more apparent than real, inasmuch as the persons who had primary immunity only were in a group who had basic immunization at a relatively long period back.

TABLE 3.—*Levels of Tetanus Antitoxin Observed at Various Intervals Following Immunization or the Last Booster Injection*

	Time from Last Antigenic Stimulus									
	0-3 Yr.		4-8 Yr.		9 or More Years		Miscellaneous		Total	
ATU Titers	No.	%	No.	%	No.	%	No.	%	No.	%
<0.01	..	....	3	7.3	3	4.8	2	2.9	8	3.7
<0.1	..	....	10	24.4	23	36.0	9	13.2	42	19.7
<0.3	11	27.5	14	34.2	20	31.2	31	45.6	76	35.6
<1	11	27.5	9	22.0	13	20.4	8	11.8	41	19.2
1.0 or >	18	45.0	5	12.2	5	7.8	18	26.5	46	21.6
Total	40	100.0	41	100.1	64	100.2	68	100.0	213	99.8

TABLE 4.—*Late Levels of Tetanus Antitoxin Observed According to the Type of Immunization Experience*

	Type of Immunization									
	Primary Only		Primary + 1 Booster		Primary + 2 or More Boosters		Miscellaneous*		Total	
ATU Titer	No.	%	No.	%	No.	%	No.	%	No.	%
<0.01	3	13.0	2	2.4	1	2.2	2	3.3	8	3.8
<0.1	10	43.5	18	21.7	6	13.0	8	13.1	42	19.7
<0.3	5	21.7	29	34.9	12	26.1	30	49.2	76	35.7
<1	4	17.4	20	24.1	9	19.6	8	13.1	41	19.2
1. or >	1	4.3	14	16.8	18	39.1	13	21.3	46	21.6
Total	23	99.9	83	99.9	46	100.0	61	100.0	213	100.0

* Those with no record of booster, but service which may have led to boosters (includes 4 with only primary observation).

‡ These figures do not appear in the tables.

The differences between those who have had one booster and those having had more than one booster following primary immunization are not so great.

The group labeled miscellaneous, which includes those persons who belong in the uncertain category as to their secondary toxoid stimuli and a small number who had their last preceding antigenic stimulus four, five, or six years before, shows levels which are intermediate between those groups who have had primary immunization only and those who have had one booster. This difference in their behavior from the group who received primary immunizations only is another justification for their separation as a group.

In Table 5 are shown the levels of antitoxic immunity observed in the group as a whole at 6 to 7 days and at 13 to 14 days after their stimulation. These results are also arranged in a manner which shows the response at these two periods according to the level of antitoxic immunity before the stimulus. From this Table it is clear that persons in this group with few exceptions responded very satisfactorily within a period of 6 to 7 days after the booster immunization, with the exception of only three, who all failed to attain levels of from 0.3 ATU per milliliter. Two persons showed levels which were between 0.01 and 0.1 units per milliliter. One showed a level between 0.1 and 0.3 ATU units per milliliter. Of the group of 208 subjects, 90% showed levels of 1.0 or more units per milliliter by the sixth or seventh days.

By 13 to 14 days after the stimulus, 205 out of 206 persons showed levels of one unit or more per milliliter. The single exception to this degree of response was in one person who showed a level between 0.1 and 0.3 units per milliliter. Further comment about this will be made later in respect to the type of stimulus used.

Simple inspection of the data will show that the titration of the sera at a level of one or more units per milliliter does not represent the maximum degree of the response. So many of the group reached this level that many of them must have had higher levels. To gather some idea of the levels which might be encountered, 25 sera showing one or more units per milliliter were run for higher levels of tetanus antitoxin. These supplementary observations were carried out after the completion of the routine tests, and sera were selected simply because satisfactory amounts were available. By happen-

TABLE 6.—*Levels of Tetanus Antitoxin Observed in Twenty-Five Persons Who Had Tests at Levels Higher Than One Unit*

ATU Titer	Fluid Toxoid	PPT Toxoid	Total
< 10.	9	8	17*
<100.	5†	2‡	7
100 or >	1§	..	1

* All at 6-7 days after booster.
† Two at 6-7 days.
‡ One at 6-7 days and one at 13-14 days.
§ At 13-14 days (had 0.01 on preliminary test).

TABLE 5.—*The Influence of Persisting Antibody Levels on the Response to the Booster Injection*

Titers Before Stimulating Injection		Response Titers: 6-7 Days After Stimulations: No.	<0.01	<0.1	<0.3	<1	1 or >	13-14 Days After Stimulation: <0.01	<0.1	<0.3	<1.	1. or >
<0.01	.....	7	0	1	0	2	4	0	0	1	0	6
>0.01	<0.1.....	40	0	0	0	12	28	0	0	0	0	39*
>0.1	<0.3.....	74	0	1	1	1	71	0	0	0	0	74*
>0.3	<1.	41	0	0	0	2	39	0	0	0	0	41*
1.0 or >	.....	46	0	0	0	1	45	0	0	0	0	45*
Totals	.....	208†	0	2	1	18	187	0	0	1	0	205

* Two persons had Q.N.S. for 3d titrations.
† Six persons, not included here, who were Q.N.S. on 1st titration all showed >1. ATU on both titrations after stimulation.

stance most of the sera selected were taken six or seven days after the stimulus. The higher levels of tetanus antitoxin observed in this group are shown in Table 6.

Seventeen of the 25 showed levels between 1 and 10 units of antitoxin per milliliter. All of the persons in this group had the tests run at the 6- to 7-day interval, and had the tests been run at 13 to 14 days, probably much higher levels of antitoxin would have been observed. Of the 7 persons who had antitoxic immunity levels between 10 and 100 units, two were tested at the 6- to 7-day period and five were tested at the 13- to 14-day interval. Five out of eight persons tested at 13 or 14 days had antitoxin in excess of 10 units per milliliter, and one had more than 100 units per milliliter.

Such high levels of antitoxin, while not of as great importance from the viewpoint of preventing tetanus, as they are far in excess of the needed amount for protection, are of significance from the viewpoint of the persistence of immunity. Such persistence is a function of the height of antitoxin attained and an individual constant.[7] Therefore, persons who attain very high levels of antitoxin are protected for relatively long periods of time. The design of studies as a whole unfortunately does not enable us to envision the ultimate levels of antitoxic immunity which can be attained.

In other studies it has been shown that passive immunity may interfere with the development of active immunity.[4]

An inspection of Table 6 shows no evidence that the persistence of high levels of actively stimulated tetanus antitoxin inhibit the capacity of a person to respond to a booster injection.

Another objective of the study is the evaluation of the capacity to respond to booster immunization at long intervals after primary or secondary immunization. In Table 7, the responses are arranged according to the time elapsed in between previous antigenic stimuli and the present experience.

As was previously noted, those who had had an antigenic stimuli in the last three years have high levels of persistent antitoxic immunity, and all of these persons, with a single exception, responded promptly with an increase of antitoxin levels. The exception in the group was one person who had more than one unit reported on the preliminary titration and who at six to seven days showed 0.1 to 0.3 ATU.

In the group who had had an interval of seven to eight years elapsing from their last antigenic stimulus, all responded promptly with a significant increase in the level of antitoxin. Forty-one out of 43, or 91%, showed levels of one unit or more six to seven days after their booster.

In the group in which nine or more years had elapsed from their last previous antigenic stimulus, two persons did not show an increase in antitoxic immunity within six to seven days. Both of these had persisting levels of immunity high enough to protect

TABLE 7.—*Tetanus Antitoxin Levels Observed Before and After Stimulation According to the Time Elapsing After Primary Immunization or the Last Booster Injection*

	Elapsed Time											
	0-3 Yr.			7-8 yr.			9 or More Yr.			Miscellaneous		
A.T.U. Levels	Before Stim.	6-7 Days	13-14 Days	Before Stim.	6-7 Days	13-14 Days	Before Stim.	6-7 Days	13-14 Days	Before Stim.	6-7 Days	13-14 Days
<0.01	..	..	..	3	..	..	2	..	..	2	..	..
<0.1	..	..	..	10	..	..	23	2	..	7	..	..
<0.3	11	1	..	14	1	..	20	..	..	29	2	1
<1.0	11	..	..	9	1	..	13	7	..	8	7	..
1.0 or >	18	40	41	5	41	43	5	54	62	18	57	64
Q.N.S.	1	..	..	2	..	..	..	..	1	3	..	2

them against infection; one of them showed a regression from the level of between 0.3 and 1.0 ATU to a level of between 0.1 and 0.3 ATU on the second test. Even in this group all persons showed protective levels of tetanus antitoxin at six to seven days after their booster injection, and 35% of them showed levels of one unit or more six to seven days after stimulating injection.

The miscellaneous group, those not classifiable as to the exact time interval following their last stimulus, behaved in a manner which conforms with the balance of the information, 85% of them showed high levels of antitoxic immunity six to seven days after their booster injection.

material has been arranged according to the type and dose of toxoid used for the booster stimulus. The subjects in these various groups were chosen at random before the accumulation of any data concerning their previous tetanus immunization. Roughly, the groups are comparable except that there were no subjects with the lowest of persisting tetanus antitoxin in the group given the smallest dose of fluid toxoid and there was relative excess of such subjects in the group who received 0.5 cc. of adsorbed toxoid.

The responses at six to seven days are somewhat inferior in the group who received 0.5 ml. of adsorbed toxoid when contrasted with those who received fluid toxoid or even

TABLE 8.—*Tetanus Antitoxin Levels Observed After Stimulation According to the Type and Dose of Toxoid Used**

	Fluid Toxoid						Adsorbed Toxoid					
	0.25 Ml.			0.5 Ml.			0.25 Ml.			0.5 Ml.		
ATU Titer	Prelim.	6 or 7 Days	13 or 14 Days	Prelim.	6 or 7 Days	13 or 14 Days	Prelim.	6 or 7 Days	13 or 14 Days	Prelim.	6 or 7 Days	13 or 14 Days
0.01	..	..	..	2	..	..	2	..	..	3	..	..
0.1	18	..	..	12	..	..	8	..	..	7	2	..
0.3	19	..	..	20	..	..	18	..	..	17	2	1
1.	11	2	..	10	5	..	9	6	..	11	5	..
1. or >	11	53	53	9	49	54	15	47	51	11	43	51
Q.N.S.	1	..	1	1	..	..	1	..	2	3	..	..
Total	55	..	..	54	..	..	53	..	..	52	..	..

* Six persons, Q.N.S. on 1st, all showed 1 or > ATU on 2d and 3d tests.

The single person who did not have one or more units per milliliter two weeks after the stimulating injection was a 44-year-old white man who had been in the service only a matter of four months from the time of his induction to discharge, and he did not have a booster injection of toxoid at any time. His stimulating injection was 0.5 ml. of adsorbed toxoid. His preliminary titer showed less than 0.01 ATU, and at six to seven days after stimulation he showed less than 0.1 ATU and on the final titration between 0.1 and 0.3 ATU.

One of our important interests in carrying out the study was to determine how much the type and dose of toxoid given for the booster injection would influence the speed and degree of response. In Table 8 the

a smaller dose of adsorbed toxoid. It should also be noted, and this is not apparent from the Table, that there were two persons who received 0.5 ml. of adsorbed toxoid who failed to show an increase in antitoxin at the end of six to seven days. One of these showed the same level at six to seven days as on the preliminary tests, and the other one showed a decrease of one step from a level of 0.3 to a level between 0.01 and 0.1 ATU per milliliter. Except for this relative slowness of response in the group receiving 0.5 ml. of adsorbed toxoid, the differences are not important.

Another factor of interest to immunologists and public health groups is the reactions which may occur when large groups of people are given booster immunizations. In

this study there were only seven persons who reacted to a sufficient degree that their reactions should be recorded and classified. Two of these were general reactions in which the patient showed moderately severe symptoms within a few hours after receiving the stimulating dose. One of these persons had experienced a similar reaction following a booster injection given while he was in the military service, but failed to mention this when he was questioned for setting up the test. Of the five local reactions, two were severe, one moderately severe, and two mild. These consisted of painful indurated areas of swelling at the site of the injection. No one developed abscesses, and there were no persistent painful nodules.

There were many in the group who received fluid as well as those who received the adsorbed toxoid who showed small but relatively asymptomatic areas of induration at the site of the injection which persisted for as long as two weeks after the injection. Generally speaking, there was no significant difference noted between the reactions with fluid toxoid or adsorbed toxoid or whether the dose was 0.25 or 0.5 ml.

GENERAL COMMENTS

The results of this study show that all persons receiving an approved tetanus immunization maintain levels of 0.1 ATU per ml. for more than three years and possibly for as long as six years. This is presumably an adequate protective level. Of the group tested at periods from 7 to 13 years after their last antigenic stimulus, 70% maintained such a protective level, and only 5% of this group had levels so low as to be considered critical in affording protection. High levels of persisting tetanus antitoxin have also been observed in infants and children immunized against tetanus.[4]

However, it should be pointed out that the persistence of antitoxic immunity in a person is of secondary importance when considered in comparison to the person's capacity to respond adequately and promptly to a stimulus, either in the form of a new injection of toxoid or a definite clinical infection with C. tetani.

Recently,[8] it has been pointed out from the morbidity and mortality statistics of tetanus in the state of Massachusetts that veterans who have been immunized as long as 10 years ago are apparently enjoying protection from clinical tetanus, as judged on the basis of the relative decrease in tetanus among the age groups who would have been immunized during their war experience.

It is of interest to speculate whether or not a person who has had an adequate primary immunization with present-day toxoids together with one or more boosters could ever be infected with C. tetani.‖ It is unlikely that this postulate will ever be tried in direct experiments with human subjects, though further analyses or morbidity and mortality tables may support the thesis.

It is reported from various sources that approximately half of all of the cases of clinical tetanus in civilian practice occur in persons without lesions which can be considered to have etiologic significance.¶ Among military personnel during World War 2 there were no doubt many who were exposed to tetanus infection by wounds deemed too trivial by the person to require attention and therefore not treated by a protective stimulating dose of toxoid. Among these there must have been some who had low levels of antitoxin because they were poor responders or because they had had a relatively long interval from their primary immunizations, to a point where they would have had subprotective levels of tetanus antitoxin. The complete absence of clinical cases of tetanus among the military personnel under such circumstances is a matter of record[10] and seems to support the thesis that the recall capacity of the person may in itself serve as a protection against clinical tetanus.

‖ While such cases have been reported, they were in the early days of tetanus immunization and before antigenic preparations were equivalent in potency to today's preparations.

¶ References 4 and 9. Peterson, J. C., and Christie, A.: Unpublished data.

However, persistence of antitoxin or ability to respond to infection is of secondary importance to a consideration of the person's capacity to respond to a stimulus with toxoid at a relatively long interval after primary immunization. Inspection of the data clearly indicates that people maintain a good capacity to respond to recall immunization up to as long as 10 or 11 years after primary immunization or the last stimulating injection of toxoid. The responses in all groups, both with respect to the elapsed time and regardless of the size of dose or type of toxoid used for stimulation, were entirely adequate to provide protection within 6 to 7 days following the stimulus.

Comparison of the four stimuli used showed no great differences. In those persons with a time interval of nine or more years, the response appears to be more prompt with fluid than with adsorbed toxoid. This has been suggested in other studies.[11] Only two persons in the group tested had borderline responses at six to eleven days after their booster injection. One of these is suspected of the possibility of not having had adequate primary immunization and certainly had had no booster immunization in the nine years intervening from his primary immunization. The other person had a protective level of antitoxin before the stimulating injection, and the borderline response at six days represented a decrease in his circulating antitoxin.

It seems clear from this study that persons who are not in shock are able to respond adequately to stimulating injections of tetanus toxoid at any time within 11 years after an approved tetanus immunization or the last antigenic stimulation.

Certainly there appears no reasonable justification, except the presence of extreme and prolonged shock, for giving prophylactic tetanus antitoxin to a person who has previously received an approved immunization against tetanus.

The superior immunity shown in this study by those who had received one or more booster injections would make it seem desirable in all instances to give a booster injection sometime within the first five years after the primary immunization. After that period it would seem entirely adequate to give tertiary or later immunization boosters not oftener than every 10 years.

An exception to this generalization might be made in the case of infants where it seems desirable to give a multiple booster one year after the primary immunization and to give a tertiary multiple booster injection prior to their entry into school at 6 years of age.

There appears to be very little to justify giving stimulating injections for possible exposures in persons who have completed primary immunization and had a booster in the past three years. Until more is known, boosters for cause should be given in the 3-to-10-year interval.

The finding of more than 100 ATU per milliliter, in one person who had received multiple stimulating injections raises a theoretical and possibly practical question as to whether or not tetanus antitoxin of human origin might be made available for prophylaxis in those instances where a person is exposed to tetanus without the benefit of previous immunization and for the treatment of clinical tetanus, especially in those known to be allergic.

SUMMARY AND CONCLUSIONS

The tetanus antitoxin levels present in 213 persons at time varying from 2 to 13 years after primary immunization or a stimulating dose of toxoid have been determined and are discussed. The majority of these persons showed residual tetanus antitoxin at a level which would protect them against tetanus infection.

The ability of a person to respond to a stimulating dose of tetanus toxoid 2 to 11 years following primary immunization or a stimulating immunization has been determined. All persons tested showed an adequate recall response.

A lapse of as many as 10 years following an antigenic stimulus does not materially

affect the capacity of a person to respond to a stimulating injection of tetanus toxoid.

Quantities of toxoid as small as 0.25 ml., either fluid or adsorbed, provide an adequate antigenic stimulus.

No significant differences in reactions were noted as to the dose and type of toxoid used.

The implications of these studies are discussed, and routines to be followed in the prevention of tetanus are suggested.

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Corticotropin and Cortisone in Rheumatic Fever

Preliminary Report of the Effect on the Electrophoretic Patterns of Plasma or Serum Proteins of Children

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INTRODUCTION

A great deal of evidence points to Group A hemolytic streptococci as being related to the cause of rheumatic fever.[1] This does not explain, however, why only certain children develop the disease after having had streptococcal infections. It is well known that there is a high familial incidence present and that heredity may play a role. In addition, evidence is accumulating to show that the highest incidence of the disease with more serious complications occurs in children whose general health is suboptimal prior to the onset of the disease. Our research, therefore, has been directed toward the host factor, and inasmuch as we have been primarily interested in nutritional and metabolic studies, the problem has been approached from this standpoint. Studies in this clinic have shown that protein metabolism is altered, and the electrophoretic analysis of plasma or serum proteins of patients with rheumatic fever provides a sensitive laboratory test which reflects the course of the disease.[2]

In recent years there has been considerable interest in the therapeutic effect of corticotropin (ACTH) and cortisone (11-dehydro-17-hydroxycorticosterone) in rheumatic fever. For this reason it was felt that observations of the changes in the protein fractions of the blood during hormonal therapy would increase our knowledge of the actions of these drugs and provide added insight into the pathological physiology of the disease.

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REVIEW OF LITERATURE

Serial electrophoretic analyses of plasma or serum proteins of 77 children with definite rheumatic fever treated with standard nonspecific methods in relation to the stages of the disease were reported by this clinic.[2] Table 1 shows the results of this study as well as normal values for children obtained by Knapp and Routh in the same laboratory.[3]

Olhagen [4] has studied the electrophoretic patterns of the proteins of children with rheumatic fever and reported results similar to those found in this clinic. He did not use the Jones criteria for diagnosis, but divided his patients into two groups, simple acute polyarthritis and a complicated group with additional heart involvement or involvement of other organs. He then found that, although gamma globulin is elevated in the complicated group, it is not elevated in the uncomplicated group.

A number of studies have appeared recently in the literature concerning the effect of corticotropin and cortisone on rheumatic carditis. Two of the most recent reports * concluded that a sufficient period of time had not yet elapsed to permit any degree of certainty that valvular deformity is prevented. At present, studies of this problem are being conducted in United States, Great Britain, and Canada by the Council of Rheumatic Fever of the American Heart Association in conjunction with the British Medical Research Council. In a preliminary re-

* References 5 and 6.

port [7] based on the analysis of approximately 300 cases, it was believed that the patients had not been under observation sufficiently long to provide any information on the prevention of rheumatic heart disease.

Mason and others [8] administered corticotropin to a normal human subject and found that there was no change in either the quality of serum proteins or their quantity as demonstrated by electrophoresis. On the basis of this report we believe that the alterations of the electrophoretic pattern by hormonal therapy are related to the therapy and the clinical course of the disease. It has been shown further in this clinic that children with rheumatic fever in the inactive stage of the disease are capable of normal protein metabolism.[2]

No report of the effect of hormonal therapy on the electrophoretic patterns of a large group of patients with rheumatic fever has come to our attention, although results based on a few cases have been published. McCarthy [9] studied the effect of cortisone on the electrophoretic pattern in certain pathological conditions, including rheumatic fever and rheumatoid arthritis. He reported that the plasma of two patients with rheumatic fever treated with cortisone showed no significant change. Videbæk and others,[10] using a salt-precipitation technique, observed that in a patient with rheumatic fever treated with 400 mg. of corticotropin for 12 days, albumin and globulin increased. In another patient with recurrent rheumatic fever who was given 1 gm. of cortisone over

TABLE 1.—*Mean Values and Standard Deviations of Electrophoretic Analyses of Normal Children (Age Five to Seventeen Years) and Children with Definite Rheumatic Fever in the Various Stages of the Disease, Treated with Standard Nonspecific Methods**

	Percentage Composition							Total Proteins, Gm./100 Ml.
	Albumin	Alpha$_1$ Globulin	Alpha$_2$ Globulin	Beta Globulin	Fibrinogen	Gamma' Globulin	Gamma Globulin	
Normal Children								
No. patients	31	31	31	31	31	18	31	31
Mean	58.4	5.7	9.7	11.5	5.4	2.5	9.3	7.4
Standard deviation	3.56	1.88	1.44	2.94	1.80	...	2.51	0.57
Early-Acute Stage								
No. patients	10	10	10	10	7	3	10	10
No. observations	10	10	10	10	7	3	10	10
Mean	36.5	9.1	16.2	12.2	11.1	4.6	16.7	7.7
Standard deviation	5.66	1.78	3.41	1.28	2.24	...	4.73	1.0
Late-Acute Stage								
No. patients	9	9	9	9	7	3	9	9
No. observations	10	10	10	10	7	3	10	10
Mean	43.1	8.1	15.0	11.8	8.7	3.3	15.0	7.9
Standard deviation	5.56	1.85	2.94	2.46	2.22	...	3.14	1.35
Early-Subacute Stage								
No. patients	11	11	11	11	9	3	11	11
No. observations	14	14	14	14	9	5	14	14
Mean	45.3	6.3	14.5	11.6	8.9	2.4	15.7	7.6
Standard deviation	5.42	0.98	3.85	3.64	3.23	...	2.71	0.83
Midsubacute Stage								
No. patients	28	28	28	28	21	7	28	28
No. observations	35	35	35	35	20	9	35	33
Mean	51.0	6.0	11.5	11.7	7.1	2.4	13.9	7.6
Standard deviation	4.69	1.62	2.29	2.64	1.21	0.90	2.82	0.75
Late-Subacute or Early-Inactive Stage								
No. patients	31	31	31	31	24	6	31	27
No. observations	37	37	37	37	29	8	37	33
Mean	53.8	5.5	10.6	12.7	6.4	2.2	12.2	7.8
Standard deviation	3.82	1.09	1.71	2.62	1.51	0.39	2.65	0.92

* The time interval from onset of the disease to the various divisions of the subacute stage are as follows: early, median 1.8 months; mid, median 3.3 months; and late, median 4.2 months.

11 days, albumin decreased and globulin increased.

Nonspecific heat-labile hyaluronidase inhibitor is known to be increased significantly during the acute phase of many diseases, including rheumatic fever. Dorfman and Moses [11] report that hyaluronidase inhibitor rapidly diminished when corticotropin was given to a patient with rheumatic fever. It rises, however, when treatment is discontinued, paralleling the decrease and increase in the erythrocyte sedimentation rate and the patient's clinical course. They suggest that corticotropin may change the state of connective tissue so that it no longer reacts to the precipitating stimuli in diseases of connective tissue.

MATERIALS AND METHODS

This study is based on the electrophoretic analyses of the protein of 24 plasma or serum samples of nine children with definite acute rheumatic fever. All of these patients were treated either with 1 to 1.5 mg. corticotropin per pound (0.5 kg.) of body weight per day or 200 to 300 mg. per day of cortisone, depending on the size of the patient. The dosage was decreased gradually and discontinued in 4 to 10 weeks.

Blood for electrophoretic analyses was obtained prior to therapy from all patients in the early or the late-acute stage of the disease. Additional samples were taken at later stages in the disease. Each protein fraction of the electrophoretic pattern is reported on a percentage basis.

The plasma or serum was diluted with three volumes of a barbiturate buffer (pH 8.6 ionic strength 0.1) and dialyzed in Visking casings at 2 to 6 C for three days with daily change of buffer. Electrophoresis was carried out in the Longsworth modification of the Tiselius apparatus with use of the long-center sections analytical cell. The current was maintained at a value of 25 ± 0.5 ma. for 120 ± 1 minute. The patterns were photographed, and projections (× 2.5) were traced on bond paper. The area enclosed by the baseline and the protein peaks was measured separately to determine values for individual components. Mobility measurements were made from the center of the boundary anomaly of each pattern.

Serum mucoproteins also were determined. Mucoprotein tyrosine was measured by a slight modification of the Winzler method.[12] The erythrocyte sedimentation rates were determined by the Westergren method, employing a uniform period of time, 45 minutes.[13]

PRESENTATION OF MATERIAL

Nine children, ranging from 4 to 10 years of age, were studied. Eight were undergoing their first attack of rheumatic fever, one her second attack. All of these children were first observed in the acute stage of the disease. The time from onset of symptoms and signs until the patient was seen in our hospital ranged from 2 to 28 days, the average time was 10 days. The physical examination of each patient revealed an acutely ill child with some evidence of carditis. In five patients the heart definitely was enlarged on radiological examination according to the standards used.[14]

Corticotropin (ACTH), 1 mg. per pound of body weight per day, or cortisone, 300 mg. per day, was administered as soon as the diagnosis of rheumatic fever was established definitely. The dosage of these drugs was decreased gradually and discontinued 4 to 10 weeks later. The average length of time of hormone administration was six weeks.

There was prompt clinical improvement in all the patients within a few days after hormones were administered. Seven patients showed evidence of cardiac residual at the time of discharge or at subsequent follow-up visits.

The electrophoretic analysis of the serum or plasma proteins of these patients on admission, 1.5 to 3.5 weeks later, and 5 to 9 weeks after admission, and mean values, are presented in Tables 2, 3, and 4.

GENERAL COMMENT

For purposes of comparison and simplicity of comment, the mean values of the various components of the electrophoretic patterns presented in Tables 2, 3, and 4 will be used as reference. They will be compared to the values in Table 1, which will be designated as the control group hereafter. It is necessary to compare these patients with the control group with respect to time because hormonal therapy distorts the commonly accepted clas-

TABLE 2.—*Values of Electrophoretic Analyses of Children with Definite Rheumatic Fever Determined on Admission and Before Patients Were Treated with Corticotropin or Cortisone*

Patient	Interval from Onset, Days	Percentage Composition							Total Proteins, Gm./ 100 Ml.	E.S.R., Mm./ 45 Min.	MPT.,* Mg./ 100 Ml.
		Albumin	Alpha$_1$ Globulin	Alpha$_2$ Globulin	Beta Globulin	Fibrinogen	Gamma' Globulin	Gamma Globulin			
L. F.	4-5	33.8	11.9	22.9	13.4	...	3.6	14.4	7.9	108	...
F. S.	5	43.3	8.4	15.9	13.7	...	2.6	16.1	8.1	105	9.2
G. B.	10	36.4	7.8	15.7	14.4	...	5.3	20.4	7.5	123	10.0
M. J. G.	14	37.3	8.5	14.8	13.7	...	3.2	22.0	8.5	105	5.5
J. H.	14	27.5	13.2	18.6	13.5	...	3.9	23.3	7.3	125	7.5
P. B.	18	47.0	8.8	15.2	10.1	...	1.7	17.2	7.4	85	9.2
H. H.	20	49.9	9.0	20.4	11.0	...	2.0	7.7	7.2	55	7.0
G. A.	28	34.8	9.6	16.3	10.5	11.6	...	17.2	7.0	82	11.8
D. R.	20	41.6	9.2	17.9	12.3	...	1.5	17.5	...	120	11.0
Mean values.....		39.1	9.6	17.5	12.5	...	3.0	17.3	7.6	94.3	8.9

* Mucoprotein tyrosine.

TABLE 3.—*Values of Electrophoretic Analyses of Children with Definite Rheumatic Fever Determined Two to Four and One-Half Weeks After Initiation of Treatment with Corticotropin or Cortisone*

Patient	Duration of Hormone Therapy, Wk.	Percentage Composition							Total Proteins, Gm./ 100 Ml.	E.S.R., Mm./ 45 Min.	MPT.,* Mg./ 100 Ml.
		Albumin	Alpha$_1$ Globulin	Alpha$_2$ Globulin	Beta Globulin	Fibrinogen	Gamma' Globulin	Gamma Globulin			
F. S.	3	52.7	6.3	12.2	13.2	...	2.4	13.2	8.4	12	6.4
G. B.	3.5	53.5	5.5	12.9	12.7	...	3.8	11.6	8.7	3	5.5
M. J. G.	3	49.9	9.2	15.0	13.7	...	2.5	9.7	7.1	5	6.0
J. H.	3	54.6	4.1	9.2	15.6	...	0.9	15.6	7.4	16	5.4
P. B.	2	49.2	7.7	13.9	13.2	...	1.7	14.3	8.4	11	6.2
H. H.	2.5	54.6	7.4	13.7	12.0	...	2.3	10.0	8.4	2	5.0
G. A.	3	50.5	5.8	16.9	17.5	7.4	...	6.8	6.2	2	9.0
D. R.	4.5	55.3	6.7	13.6	13.9	...	0.4	10.1	...	5	3.5
Mean values	3.1	52.5	7.4	13.4	14.0	7.4	2.0	11.4	7.8	7	5.9

* Mucoprotein tyrosine.

TABLE 4.—*Values of Electrophoretic Analyses of Children with Definite Rheumatic Fever Determined Five to Nine Weeks After Initiation of Treatment with Corticotropin or Cortisone*

Patient	Duration of Hormone Therapy, Wk.	Percentage Composition							Total Proteins, Gm./ 100 Ml.	E.S.R., Mm./ 45 Min.	MPT.,* Mg./ 100 Ml.
		Albumin	Alpha$_1$ Globulin	Alpha$_2$ Globulin	Beta Globulin	Fibrinogen	Gamma' Globulin	Gamma Globulin			
L. F.	8	52.6	7.0	14.0	12.8	...	2.9	9.7	7.8	18	...
F. S.	9	55.7	5.3	12.2	13.8	...	3.2	9.8	6.8	5	3.8
G. B.	5	55.0	6.8	13.6	13.6	...	0.7	10.3	7.0	10	5.5
M. J. G.	9	59.3	6.3	9.6	12.7	...	0.6	11.5	...	15	4.5
J. H.	6	62.2	5.6	10.0	10.5	...	0.7	11.0	...	8	5.0
P. B.	7	51.7	5.9	14.1	11.6	...	2.8	13.9	8.2	20	4.0
H. H.	7	56.5	8.7	11.2	13.3	...	1.6	8.7	8.0	10	6.0
G. A.	6	55.6	6.3	15.5	13.7	...	1.8	7.2	8.0	15	9.0
D. R.	..	....	...	....	....	...	...	....	...	..	...
Mean values	7	56.1	6.5	12.5	12.7	...	1.9	10.2	7.1	12.1	5.4

* Mucoprotein tyrosine.

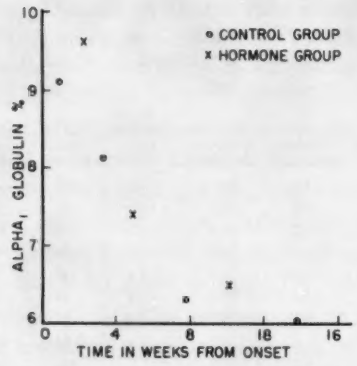

Fig. 1.—Comparison of the alpha$_1$ globulin component in the control group and the hormone-treated group. Mean values at various intervals of time after onset of the disease. Normal value is 5.7%.

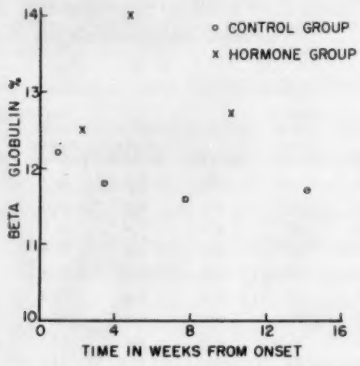

Fig. 3.—Comparison of the beta globulin component in the control group and the hormone-treated group. Mean values at various intervals of time after onset of the disease. Normal value is 11.5%.

sification of the stages of the disease, and therefore we have no accurate method of determining exactly the stage of the disease at any given time during hormonal therapy. The differences in mean values were evaluated statistically by obtaining the critical ratio *t*. The *t*-test for related measures was obtained when the same patients were in the two groups compared. Figures 1, 2, 3, and 4 demonstrate graphically the comparison of the response of alpha$_1$, alpha$_2$, beta, and gamma globulin to the two therapeutic regimens. We realize that additional data would be helpful to clarify the rate of change, and we recommend that serial electrophoretic analyses be done on admission, the day before hormonal therapy is begun, every three days for two additional determinations, and at weekly intervals until the mucoproteins reach the normal range.

Total Protein.—Total protein does not appear to be affected significantly by corticotropin or cortisone. The mean values at the various time intervals are similar to comparable times in the control group. It was also concluded that nonspecific therapy did not affect total protein significantly.[2]

Albumin.—All but two of the patients in this study had a markedly decreased albumin level, corresponding closely to the values obtained in the control group in the acute stage of the disease. In all of the patients except these two there was a marked increase in albumin shortly after corticotropin or corti-

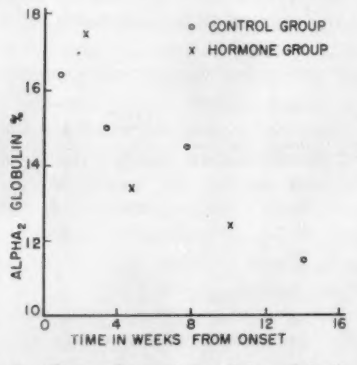

Fig. 2.—Comparison of the alpha$_2$ globulin component in the control group and the hormone-treated group. Mean values at various intervals of time after onset of the disease. Normal value is 9.7%.

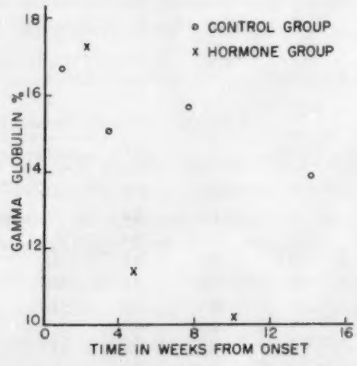

Fig. 4.—Comparison of the gamma globulin component in the control group and the hormone-treated group. Mean values at various intervals of time after onset of the disease. Normal value is 9.3%.

sone administration was begun. A mean value of albumin taken between 1.5 and 3.5 weeks after initiation of hormonal therapy corresponds to the value obtained in the midsubacute stage of the control group. The midsubacute stage was not reached on the average until 3.3 months after the onset of the disease. Although normal values for albumin were not attained until the early inactive stage of the disease in the control group (mean interval after onset 4.2 months), they were reached by 5 to 9 weeks in this group.

It is known that the plasma proteins of patients with rheumatic fever exhibit a hyperglobulinemia rather than a hypoalbuminemia. Therefore, since our values are reported in percentage of the total, the initial decrease in albumin is probably a compensatory decrease. Furthermore, the rapid return to normal may be a manifestation of a rapid decrease in certain of the globulin components as will be evidenced by subsequent discussion.

Alpha$_1$ Globulin.—All the patients in this study showed an elevated alpha$_1$ globulin in the acute stage of the disease. This elevation was very transient in our patients, decreasing to near normal values within 1.5 to 3.5 weeks after initiation of therapy in all the patients except one. A similar early elevation and rapid decrease to normal was observed in the control group, although our results indicate that the return to normal is more rapid in the hormone-treated group.

Hyaluronidase inhibitor and C-reactive protein also decrease rapidly in the presence of hormonal therapy.† These observations suggest that alpha$_1$ globulin may be related to the acute-phase reactors.

Alpha$_2$ Globulin.—This component was elevated markedly in the acute stage of the disease in this group of patients as well as in the control group. It is significant that in the present group this fraction tended to remain elevated throughout the course of the disease. A similar observation was made in the control group where it was noted that alpha$_2$ globulin decreased gradually as the disease regressed.[2] A mean value at five to nine weeks after hormonal therapy was begun shows alpha$_2$ globulin to be elevated and corresponding to the value in the midsubacute stage of the control group. At that time the mucoprotein tyrosine was still elevated, although the erythrocyte sedimentation rate was normal.

The close correlation between alpha$_2$ globulin and mucoprotein tyrosine suggests that this fraction of the plasma proteins may contain the serum mucoproteins. The data presented in this study show that, aside from an initial drop, hormones have little effect on the mucoprotein tyrosine or alpha$_2$ globulins beyond that which is produced by nonspecific therapy. Data from our laboratory suggest that alpha$_1$ globulin contains part of the serum mucoproteins.[12]

It is suggested then that the alpha$_2$ globulin fraction may possibly be related to the proliferative processes of the disease because of its slow gradual return to normal. Other studies ‡ indicate that the serum mucoproteins are a measure of rheumatic activity. If this is true—and further investigation is certainly necessary—then it is probable that hormonal therapy does not alter significantly the proliferative processes of rheumatic fever. However, most of our patients could not be studied or treated within hours or even one to two days after the onset of their disease. Additional data must be accumulated on such patients before one can say with any degree of certainty that shortening of the acute processes of the disease may not also have a beneficial influence on the chronic changes.

Beta Globulin.—In the present study the response of beta globulin to hormonal therapy appears to be significantly different from the response of this component to nonspecific therapy. In the control group there was no correlation between this component and the stage of the disease. In this study, a slight elevation early in the disease persisted or became more elevated at some time during the course of hormonal therapy. Four patients

† References 15 and 16.

‡ References 15 and 17.

showed a definite elevation beyond the original elevation early in the course of treatment, one showed a gradual rise, and the other four showed a persistence of the original elevation.

Beta globulin is elevated in certain diseases and is thought to be related to the presence of a labile lipoprotein. § Other observers have found that there is an elevation in beta globulin or serum cholesterol in rats when they are given corticotropin or cortisone.‖ We have obtained electrophoretic analyses on a patient with lupus erythematosus and on another with dermatomyositis, both of whom were treated with moderately large doses of corticotropin or cortisone. In both of these children beta globulin was definitely elevated after hormones had been administered for a short time. The significance of the effect of these hormones on beta globulin cannot be explained at the present time.

Fibrinogen and Gamma' Globulin.—In the control study it was found that fibrinogen was elevated markedly in the acute stage of the disease and decreased gradually as the disease regressed. Insufficient fibrinogen levels were obtained in this study for evaluation.

Twenty gamma' globulin determinations were made in this study, and, although this component was elevated early in the disease in the control group, the mean value in the present group is within normal limits. In view of these findings it would seem to be more valuable to obtain fibrinogen rather than gamma' globulin determinations in the future.

Gamma Globulin.—Gamma globulin values were elevated markedly in the early stages of the disease in the present study as well as in the control study (Patient H. H. was the only exception to this). In the control study this fraction decreased gradually as the disease regressed. In the present study, however, gamma globulin decreased markedly soon after hormonal therapy was instituted, (with the exception of H. H.) so that it was very nearly normal within 1.5 to 3.5 weeks.

It is generally accepted that the gamma globulin reflects the presence of antibody in the serum. It has been reported that this fraction is not elevated in rheumatic fever in the absence of an antecedent illness.[22] This is not in accord with other findings. ¶ In three patients we could not obtain a definite history of an antecedent illness; all three showed an elevated gamma globulin fraction.

Reports in the literature are conflicting with respect to the effect of corticotropin and cortisone on gamma globulin. # In animal experimentation, hormones apparently cause a significant increase in total serum globulin, the increase being primarily due to an increase in beta and gamma globulin. In human experimentation, the effect of these hormones on gamma globulin is not the same as found in animals.* These studies suggest that in certain disease processes hormones cause a decrease in gamma globulin as measured by electrophoresis.

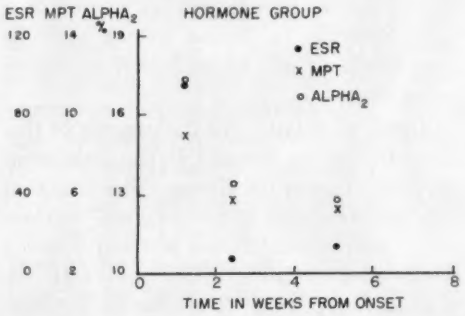

Fig. 5.—Comparison of the decrease in erythrocyte sedimentation rate (E. S. R.), serum mucoprotein tyrosine (M. P. T.), and alpha$_2$ globulin during hormone therapy. Mean values taken at various intervals of time during the disease. Baseline represents approximate normal values.

Although gamma globulin decreased markedly in the presence of hormonal therapy, it began to increase in two of our patients

§ References 18 and 19.

‖ References 20 and 21.

¶ References 2 and 23.

References 20 and 21.

* References 24-26.

after hormonal therapy was discontinued. This suggests that the inhibition of antibody formation by these hormones is very short-lived. It is suggested that, because of its marked tendency to lower the gamma globulin component, hormonal therapy primarily attacks the hypersensitivity processes of rheumatic fever.

Erythrocyte Sedimentation Rate.—The erythrocyte sedimentation rate (E. S. R.) was elevated markedly in the patients of this study before therapy was begun. It decreased toward normal very rapidly, so that a mean value taken at 1.5 to 3.5 weeks after initiation of hormonal therapy was within the low normal range. Two of our patients showed a slightly elevated E. S. R. five to nine weeks after therapy was begun, but this can be attributed to the "clinical rebound" which these patients were undergoing at that time. The mean value at that time was again within the normal range. It has been noted by many observers that the E. S. R., which is elevated markedly in the acute stage of rheumatic fever, returns to normal very quickly after hormones are administered and that its fall parallels the disappearance of fever and polyarthritis.†

Mucoprotein Tyrosine.—Mucoprotein tyrosine was elevated markedly in all of the patients in this study in the acute stage of the disease. The normal value obtained in our laboratory is 2 to 4 mg. per 100 ml., the mean in these patients on admission was 8.6 mg. per 100 ml. Mucoprotein tyrosine decreased gradually during the course of treatment, closely paralleling the fall in alpha$_2$ globulin in all the patients except two. The mean value of mucoprotein tyrosine five to nine weeks after initiation of therapy was still elevated.

Kelley, Good, and McQuarrie [29] first reported that the mucoprotein tyrosine value was elevated markedly in acute rheumatic fever as well as in other diseases. This observation has been substantiated by Levy and Jackson [12] and others. It has also been observed that the mucoprotein tyrosine gradually decreases to normal values in the subacute stage of the disease. In this clinic weekly mucoprotein tyrosine values were obtained on all patients with rheumatic fever. It is our impression that this component of the serum is a measure of rheumatic activity and is a better index during hormonal therapy than the E. S. R.

Our observations indicate that corticotropin and cortisone do not significantly affect the return of mucoprotein tyrosine to normal, as compared to nonspecific therapy, although there is an initial drop as was the case in alpha$_2$ globulin. This agrees with a recent detailed report on this subject by Kelley, Adams, and Good.[17] If the serum mucoproteins and alpha$_2$ globulin levels reflect the chronic processes of rheumatic fever, as some investigators suggest, then the value of hormonal therapy in preventing residual cardiac damage is questionable.

Course of the Disease.—The data and foregoing comment suggest that the active stage of rheumatic fever may be shortened by corticortropin and cortisone. However, serial electrophoretic analyses were not obtained after hormonal therapy was discontinued.

The mean interval of time from admission until the patients were dismissed from the hospital was 3.5 months, with a range from 8 to 17 weeks. This excludes patient H. H., who was in the hospital for 27 weeks. In the control group, the median interval from onset of the disease until the early inactive stage was reached was 4.2 months, with a range from 6 weeks to 10.5 months, excluding one patient who was in the hospital 20 months. It is seen then that the patients who received hormone therapy were confined to the hospital for a shorter period than those who received nonspecific therapy. The patients were not dismissed unless the disease was considered inactive, but it must be remembered that after hormone therapy one cannot always be certain that the disease is arrested. These patients were, however, followed on an outpatient basis, and in all the disease remained inactive after dismissal.

The preliminary report on the extensive study being conducted by the American

† References 27 and 28.

Heart Association [7] stated that there was no definite evidence that the course of the disease was shortened by corticotropin and cortisone, and no definite conclusions can be drawn from the present study. It is very important that additional data be obtained in this regard, since shortening the course of the disease could be considered an indication for the use of these drugs.

SUMMARY

Since it has been determined that electrophoretic analyses of the serum proteins exhibit a definite pattern in acute rheumatic fever, we obtained data to ascertain whether corticotropin (ACTH) or cortisone appreciably alter this pattern. The serial electrophoretic patterns of nine patients treated with hormones are presented and discussed.

Although further work must be done, our preliminary data indicate that hormonal therapy exerts a definite effect on albumin, $alpha_1$ globulin, beta globulin, and gamma globulin. The results show that the rapid return of albumin to normal is a compensatory response resulting from the decrease in the percentage of globulins.

$Alpha_1$ globulin returns to normal more rapidly than in the nonspecifically treated group. This may mean that the acute-phase reactions in rheumatic fever are shortened by hormonal therapy. Beta globulin either remains elevated or becomes even more elevated during the course of treatment. Gamma globulin decreases rapidly, sometimes to subnormal levels. This suggests that the major effect of the hormones is related to hypersensitivity processes of the disease. Hormonal therapy has little effect on the $alpha_2$ globulin or mucoprotein tyrosine. These findings make one skeptical of the value of these drugs in preventing residual cardiac damage.

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Cystic Hygroma of the Chest Wall

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Large swellings of the chest wall occur infrequently in infants and children. Regardless of whether the swelling has been present since birth with a gradual increase in size or makes a dramatic appearance with rapid growth in a short period, it is an alarming situation. For this reason and because cystic hygroma of the chest wall is unusual, I am reporting two cases operated on within a period of 15 months.

REPORT OF CASES

CASE 1.—R. P., an 8-year-old boy, was referred by Dr. Irvin S. Belgrade on Jan. 7, 1953. He had a painless swelling over the right side of the chest since birth. The parents stated that the skin over the swelling became red in color for a short while around Christmas of 1953. After that the swelling doubled in size. The past history was not unusual. On physical examination, the only abnormal finding was this large raised soft mass. It extended from two finger breadths below the right nipple to two finger breadths below the right 12th rib and from the right sternal border to the anterior axillary line. It appeared slightly lighter in color than the surrounding skin and was not movable. There was no lymphadenopathy. Urinalysis, complete blood cell count, and chest x-ray were normal.

This mass was considered to be either a fibroma or a papillary cystadenoma with malignant changes. At operation, under general anesthesia, the mass was dissected and excised from the chest wall. It extended through the dermis into a portion of the underlying muscles. No definite capsule or cleavage plane was found over most of the tumor. Several small cysts were entered during the excision, and a clear yellow fluid exuded. All of the tumor that was identified grossly was excised, including a portion of the underlying muscles. Recovery was uneventful, and the boy went home on Jan. 15, 1953.

The pathological specimen, as described by Dr. Lester S. King, consisted of three parts, the largest being a nondescript shaped piece of soft tissue measuring 8 cm. by 5 cm. by 2.5 cm. One surface consisted of brownish-red striated muscle attached to a light tan grayish-white tissue, which on sectioning contained many cysts, varying from 0.5 to 1.5 cm. in diameter and containing clear yellowish fluid. The second largest portion, also a nondescript piece of soft tissue, measured 4 cm. by 2.5 cm. by 2 cm. It presented an identical appearance to the larger one. The third specimen was an elliptical shaped piece of skin, 1.2 cm. by 0.5 cm., in the center of which was a slightly elevated light tan papillomatous-like mass measuring 0.4 cm. by 0.2 cm. On section the tumor was confined to the epidermis. The microscopic diagnosis was massive lymphangioma (cystic hygroma) of the subcutaneous tissue and lymphangioma of the skin.

CASE 2.—G. P., an 18-month-old boy, was referred by Dr. Sol P. Ditkowsky on March 28, 1954. The parents stated that the child had a small "lump" on the right side of the chest early in February, 1954. This swelling was not tender or any different in color than the surrounding skin. The "lump" grew, and the child was taken to their doctor, who aspirated the mass; it disappeared, only to return in a few days, reaching the size of an orange. On physical examination there was only this soft adherent mass on the right side of the chest, extending from the posterior axillary line to the right nipple and from the 5th to the 11th ribs. Lymphadenopathy was absent. Urinalysis, complete blood cell count, and chest x-ray were negative.

The mass was considered to be a cystic hygroma. At operation, under general anesthesia, a multilocular cyst was found attached densely and profusely to the skin, fascia, and underlying muscle. All adhesions were dissected free, and the complete mass was removed. Recovery was uneventful, and the infant went home on March 30, 1954.

The pathological specimen, described by Dr. Lester S. King, consisted of a cyst which measured 6.5 cm. by 3.2 cm.; the wall was thin, less than 0.5 mm., and the inner surface was tan to reddish-pink and finely trabeculated. The microscopic diagnosis was cystic hygroma of the chest wall, with portions of striated muscle showing partial degeneration.

COMMENT

Cystic hygromas occur in the mouth,[1] neck,[2] axilla,[3] mediastinum,* abdomen,[1] and inguinal [8] and popliteal [9] areas. There

From the Department of Surgery, Illinois Masonic Hospital, and the Loyola University, Stritch School of Medicine.

* References 4-7.

are some excellent reviews of the entire subject.† Ninety per cent of the hygromas are observed before the end of the second year of life.[11] Ninety-three per cent of all hygromas occur in the neck.[2] Gross reported 112 examples of this lesion in infants and children seen up to December, 1950. Of the cases he reported, 100 were in the neck. Of the remaining 12, 3 were in the mediastinum, 2 in the axilla, 2 in right thigh, 1 on face, 1 in left thigh, 2 in left pectoral region, and 1 in right pectoral region.

These multicystic structures have spaces lined by flattened endothelial cells. The various spaces may communicate with one another or be separate, the degree of communication depending upon the amount of pressure atrophy occurring in the septa which originally separate the loculi. Characteristically, the hygroma becomes adherent to neighboring structures and has an irregular and somewhat ill-defined outline. Aggregates of lymphoid cells and definite lymphoid follicles with germinal centers are not uncommonly present, while structures such as muscle bundles, blood vessels, and nerve fibers may apparently traverse the substance of the cystic mass.[7] The resulting swelling may reach the size of a coconut.[13] Microscopically, the picture is the same as a hemangioma, except the endothelium-lined spaces are filled with clear lymph and a few lymphocytes, instead of blood.[14]

These two cases illustrated all the peculiar characteristics described, which suggested a malignant tumor in the 8-year-old child but led to the correct preoperative diagnosis in the 18-month-old boy.

SUMMARY

Cystic hygroma of the chest wall, a rare clinical entity in an unusual location, occurred in two boys, one 8 years and the other 18 months old. The chest wall swelling was present since birth in the older boy and increased to the size of an orange after it became superficially infected. In the infant, the cystic mass appeared and swelled to the same size within a few weeks. In each the mass was completely excised and recovery was uneventful. This adds another location to those enumerated—the neck most commonly, and the mouth, axilla, mediastinum, abdomen, and inguinal and popliteal regions far less frequently—where cystic hygroma may occur.

30 N. Michigan Ave. (2).

† References 3, 7, and 10.

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Response of Small Premature Infants to Restriction of Supplementary Oxygen

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As part of a study of the role of environmental oxygen on retrolental fibroplasia in premature infants of low birth weight,[1] observations were made on the tolerance of these infants to early removal from oxygen. Because of the common occurrence of respiratory irregularities associated with immaturity of the respiratory tree, the respiratory center, and the structures of the thoracic cage and the frequent superimposition of intracranial hemorrhage at birth,[2] it has been customary to provide small premature infants with an oxygen-rich environment.[3] When evidence began to accumulate of the possible harmful effect of oxygen therapy in the causation of retrolental fibroplasia,* it became important to reexamine the necessity for this form of therapy.

PLAN OF STUDY

The routine practice in the premature nursery of the New York Hospital was to place infants with a birth weight below 1650 gm. in an incubator supplied with oxygen, regardless of respiratory pattern. When they reached or had regained a weight of 1600 gm., they were weaned to room air over a four-day period by daily gradual reduction of the liter flow rate of oxygen. For purposes of this study half of the infants (Group I) were continued on this regimen, and the other half (Group II) were removed from oxygen at an earlier age, beginning at the time of their assignment to the curtailed oxygen group. Infants were assigned to Groups I and II by means of a modified random sampling technique, at the times shown in Table 1.

For both groups, the liter-flow gauges were set at 3 liters per minute in the Gordon Armstrong incubators and at 1.5 liters per minute in the Isolettes. Weaning from oxygen was accomplished over a four-day period by reduction of the liter flow rate by one-third on the first two days, two-thirds on the third day, and completely on the fourth day. Oxygen concentrations were measured daily in the incubators, and, although the over-all range was wide, 30%-80%, the range for individual infants usually fell within 10 to 15%. Fifteen of the 99 babies were in oxygen at concentrations consistently above 50%; 26, at concentrations of 40% and less, and the remaining 58, at concentrations in the 40%-50% range. These three levels of concentration applied equally to Group I (prolonged) and Group II (curtailed oxygen).

TABLE 1.—*Time of Assignment to Study*

Birth Weight, Gm.	Day of Assignment
1000 or less	14
1001-1361	7
1362-1650	2

All infants continued to reside in the incubators until a weight of 1600 gm. was attained, the incubators serving only as heated cribs for those babies in Group II, who received no more supplementary oxygen. Babies within each weight group were paired according to type of incubator, either

From The New York Hospital-Cornell Medical Center, Department of Pediatrics.

* References 4-10.

Isolette or Gordon Armstrong, and so far as possible all other conditions of humidity, temperature control, feeding mixture and technique of feeding, use of infusions, transfusions, and antibiotics were kept constant. Funduscopic examinations were performed at regular intervals in the premature nursery and after discharge from the hospital. These results will be reported separately.[1]

To mitigate the hazard that small premature babies might die if oxygen were initially withheld, the study was originally planned so that assignment of the babies to prolonged or curtailed environmental oxygen was made at a time subsequent to the greatest expected number of deaths. Accordingly, all infants received oxygen for at least 5 days, and the smallest babies (1000 gm. and less) were in oxygen for as long as 17 days. The effect on mortality of early removal from oxygen was therefore not studied at the most crucial time, i. e., during the first 48 or 72 hours of life.

Lanman and his co-workers[10] did not believe the mortality rate was increased when small prematures were kept at atmospheric oxygen concentration from birth. In their recent study prematures between 1000 and 1850 gm. birth weight were assigned to a high- or low-oxygen environment. Those in the low-oxygen group received oxygen at concentrations below 50% only for cyanosis. The over-all mortality among the 45 babies in high oxygen was 20% and among the 40 infants in low oxygen, 30%. The percentage difference was not statistically significant.

In the present study the immediate effects of early withdrawal from oxygen were determined by frequent and careful observations on each baby, with attention to respiration, color, cry, activity, presence or absence of cyanosis, retractions, periods of apnea, and response to feedings. Rate of weight gain in the two groups while in the nursery was compared, and the need for infusions and transfusions was assessed. In some of the infants determinations of fetal and adult hemoglobin were made. These form the basis of a separate report.[11]

To assess the late effects of early removal from oxygen the babies have been followed for a minimum period of six months to as long as two and a half years. Growth in height and weight, developmental progress, and neurologic status have been observed.

GROUP ASSIGNMENTS

This study was begun on Jan. 28, 1950, and in the next 18 months 49 boys and 50 girls were assigned to it. Of the 99 babies who survived to the age for inclusion in the study, there was only one death: A group II infant with a birth weight of 1190 gm. died on the 11th day of life, before oxygen reduction was complete.

Seven of the 49 babies who were scheduled for early removal from oxygen (Group II) did not come out as planned because of presumed need for further oxygen: cyanosis, relieved by oxygen, or periods of apnea, retraction of the chest, or feeble condition with scant motor activity. Three had birth weights below 1000 gm.; two others had minimum weights below 1000 gm. at the time they were assigned to the study, and the other two were larger babies (1420 and 1580 gm.) who were in such poor condition at the age of 48 hours when oxygen reduction was scheduled that for one it was not attempted and for the other could not be completed. In the other 42 infants in Group II, early removal from oxygen was accomplished without difficulty. In the light of our subsequent experience with successful removal of babies from supplemental oxygen at still earlier ages and even of withholding it altogether, it is likely that several of the babies could have been safely removed from oxygen according to schedule. At the beginning of the study, however, we were justifiably overly cautious.

Of the seven babies in Group II who were returned to oxygen, one infant with a birth weight of 998 gm. and a minimum weight of 710 gm. at the age of 7 days tolerated reduction of oxygen at 14 days and weaning from oxygen over a 3-day period, but in the subsequent 12 hours she experienced two epi-

sodes of cyanosis, both relieved by oxygen. It was decided to resume oxygen administration.

A boy whose birth weight was 800 gm. and whose minimum weight was 600 gm. showed no difficulties during the reduction of oxygen concentration begun on the 14th day. After being out of oxygen for three and one-half days, he had three periods of apnea and duskiness, and oxygen was restarted.

A third child, who weighed 1025 gm. at birth and reached a minimum weight on the 7th day of 833 gm., was weaned from oxygen by the 10th day of life and remained in the incubator in room air for the next nine days without difficulty. Then, because of a dusky color, oxygen administration was reinstituted. In retrospect this was probably unnecessary.

RESULTS OF STUDY

The total time in oxygen, including the three days of gradual oxygen reduction, and the number of infants by weight in the various groups are shown in Table 2. The average time in oxygen of Group II infants was one-third to one-fourth of Groups I or II → I. Only one baby under 1000 gm. at birth completed the scheduled early oxygen reduction. Her birth weight was 960 gm. The minimum weight was 790 gm. at nine days, and when she came out of oxygen it was 900 gm.

Excluding the seven babies detailed above who were replaced in oxygen after an attempted early removal, no difficulties were experienced by the infants in Group II during or after the withdrawal of supplemental oxygen. The pattern of respiration of the infants in room air and that of their counterparts of like age and weight in oxygen was essentially similar; their activity was comparable, and behavior during feedings was alike. In short, there was no evidence that the babies when taken out of oxygen earlier than usual were harmed thereby.

TABLE 2.—*Days in Oxygen*

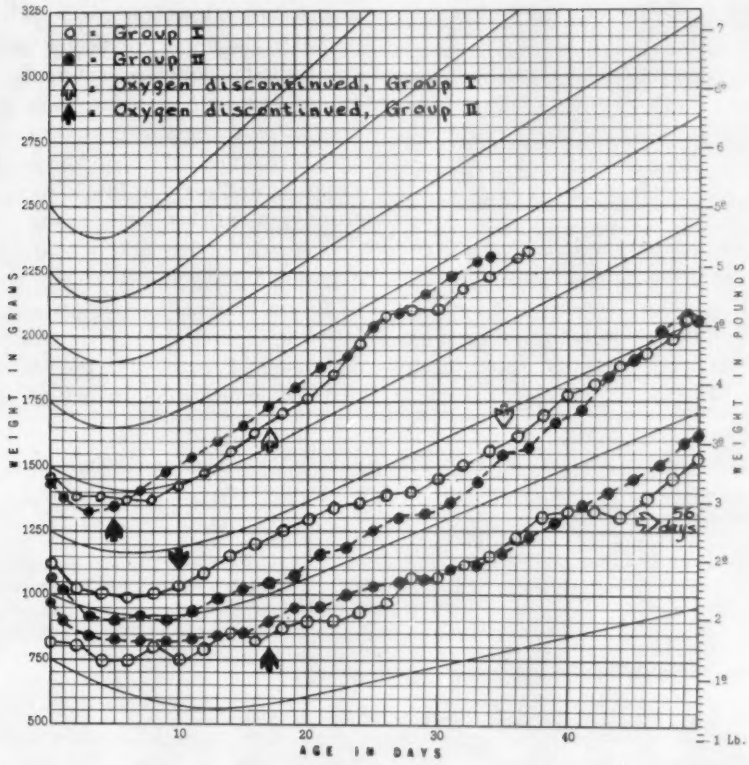
Birth Weight, Gm.	II		I			II → I		
				Days			Days	
	Babies	Days	Babies	Average	Range	Babies	Average	Range
1000 and below	1	17	5	49	47-60	3	56	53-60
1001-1361	21	10	21	33	16-52	2	45	35-81
1362-1650	20	5	24	20	8-35	2	23	20-29

During the reduction of oxygen concentration of a fourth baby, whose weight at birth was 1420 gm., apnea and irregular respirations were noted, and the liter flow rate was reset at the original level.

In the three remaining babies, reduction of oxygen concentration was not attempted because respiratory irregularities were present while receiving oxygen.

These seven infants continued to receive supplemental oxygen until a weight of 1600 gm. was attained, at which time no difficulties were encountered when they were returned to atmospheric oxygen. Thus their management after the attempt at removal from oxygen had failed differed in no way from that of the infants originally assigned to Group I, the prolonged-oxygen group. These 7 babies are hereafter referred to as Group II → I.

The rate of weight gain of small prematures is regarded as one reliable and objective guide of progress. The weight curves of the infants in Group II paralleled the expected curves for infants of similar birth weights and were indistinguishable from the weight curves of their counterparts in Group I. This point is illustrated by the accompanying graphs taken from the hospital records of three sets of paired infants in the three weight groups. The curves are typical for the infants as a whole and are plotted on the grid devised by Dancis and co-workers [12] for recording weights of premature in-



Weight curves of paired infants in three weight groups. Arrow indicates the time of discontinuance of oxygen. Note the parallel gain in weight of Group I and II infants.

fants. The time of termination of oxygen therapy is indicated by an arrow.

The need for subcutaneous infusions in the first week or more of life pending adequate oral intake of fluids was less in the Group II than in the Group I babies. Infusions were given as hypotonic saline solution in small amounts two or three times a day for dehydration or failure to accept an oral fluid intake of 100 cc/kg/day for several days. The smaller the infant, the greater was the need for parenteral fluids. All infants who weighed 1000 gm. and below at birth received infusions. Above this weight range, only 5 of 41 infants in Group II, as compared with 14 of 45 in Group I, required parenteral fluid therapy. All four babies in Group II → I in the two higher weight ranges required infusions. These observed differences may in part be related to the drying effect of oxygen, even though humidified.

The number of infants who received transfusions was higher in Group I than in Group II.

TABLE 3.—*Infants Receiving Subcutaneous Infusions*

Birth Weight, Gm.	II	I	II → I
1000 and below.....	1	5	3
1001-1361	4	10	2
1362-1650	1	4	2
	6 of 42	19 of 50	7 of 7

TABLE 4.—*Infants Receiving Transfusions*

Birth Weight, Gm.	II	I	II → I
1000 and below.....	0	3	3
1001-1361	7	11	2
1362-1650	2	4	1
	9 of 42	18 of 50	6 of 7

TABLE 5.—*Follow-Up Examinations*

Birth Weight, Gm.	Sex M	Sex F	II	I	II → I
1000 and below	3	5	1	4	3
1001-1361	17	19	15	20	1
1362-1650	16	15	11	18	2
Totals	36	39	27	42	6
	75				

In this respect too the infants in the curtailed-oxygen group fared at least as well as those with a more "conservative" oxygen regimen. The indication for transfusion was a hemoglobin level, measured spectrophotometrically, of 8.0 to 8.5 gm. per 100 ml. or less in an infant who by clinical evaluation seemed to be thriving less well than formerly. If the value leveled off or began to climb and if the infant continued to gain well and be increasingly more active, transfusions were withheld, even with hemoglobins as low as 8 to 8.5 gm. per 100 ml. Iron preparations were usually administered after discharge from the premature nursery, at the age of two and one-half to three months. The rationale for this method of management of the anemia of prematurity has been presented by Schulman and Smith.[13]

Arterial oxygen saturation, oxygen consumption, blood pressure, and measurements of respiratory function applicable to larger, cooperative subjects were not made in these tiny babies. However, careful clinical appraisal in the nursery indicates that, barring the smallest and most immature babies (1000 gm. or less at birth) and those exhibiting respiratory distress or central nervous damage, premature babies of low birth weight thrive as well early in life in room air as in an oxygen-enriched environment.

A search for late effects of the shortened exposure to oxygen was made by comparison of the infants in the two groups during a follow-up period of from six months to two and one-half years. Of the 98 survivors, pertinent information (exclusive of eye examinations, obtained on a larger number to be reported separately [1]) is available on 75 infants.

TABLE 6.—*Average Height in Centimeters*

Birth Weight, Gm.	Group	3 Mo.	6 Mo.	9 Mo.	12 Mo.	15 Mo.	18 Mo.	24 Mo.
1000 and below	I	48 (3)*	58 (6)	64 (7)	69 (4)	.....	73 (1)	79 (1)
	II	50 (1)	63 (1)	69 (1)	73 (1)	.....	79 (1)	.....
1001-1361	I	54 (14)	59 (16)	67 (12)	71 (11)	77 (3)	77 (5)	83 (3)
	II	52 (6)	60 (13)	66 (7)	73 (7)	.....	76 (5)	79 (2)
1362-1650	I	52 (17)	61 (15)	68 (14)	72 (13)	79 (2)	81 (3)	83 (1)
	II	53 (7)	64 (9)	69 (7)	73 (5)	79 (3)	79 (2)	83 (1)

* Numbers in parentheses represent the number of observations.

TABLE 7.—*Average Weight in Kilograms*

Birth Weight, Gm.	Group	3 Mo.	6 Mo.	9 Mo.	12 Mo.	15 Mo.	18 Mo.	24 Mo.
1000 and below	I	3.1 (3)*	5.5 (7)	7.0 (7)	7.6 (4)	.....	7.9 (2)	10.0 (1)
	II	2.6 (1)	6.4 (1)	7.8 (1)	9.2 (1)	.....	10.0 (1)	.....
1001-1361	I	3.5 (15)	5.8 (16)	7.6 (14)	8.7 (12)	10.0 (3)	10.5 (5)	10.5 (3)
	II	3.5 (6)	5.7 (14)	7.0 (7)	8.6 (7)	.....	9.8 (6)	11.1 (2)
1362-1650	I	4.2 (18)	6.4 (17)	8.5 (15)	9.9 (13)	11.1 (3)	11.4 (3)	12.3 (1)
	II	4.0 (8)	6.3 (10)	7.3 (7)	8.5 (7)	9.8 (3)	9.3 (2)	10.9 (1)

* Numbers in parentheses represent number of observations.

Height and weight curves were parallel for the three birth weight subgroups, irrespective of the duration of oxygen therapy while in the premature nursery. The 6 babies in Group II → I are included with the 42 babies of Group I for this portion of the analysis, since their anthropometric measurements and oxygen exposure were the same. Males and females are combined. The number in parentheses represents the number of observations. The average values for growth in length are strikingly similar, regardless of birth weight and duration of oxygen administration.

Gain in weight of the different groups at similar ages is recorded in Table 7. As in the preceding table, the measurements for males and females are combined and the number in parentheses represents the number of observations.

It is seen that by the age of 6 months the weight differences present at birth have become inconspicuous and that there is no consistent difference between the Group I and II infants in each weight subgroup.

The rate of weight gain of these infants compares favorably with the much larger number studied by Zeltner in the first 9 months of postnatal life.[14] In Zeltner's series, the average increment of increase in weight for the group whose initial weight was 1000 to 1500 gm. was 1.9 kg. from the third to the sixth month. In our infants it was 2.3 kg. (Group I) and 2.2 kg. (Group II) for the children with birth weights of 1001 to 1361 gm., and 2.2. kg. (Group I) and 2.3 kg. (Group II) for those weighing 1362 to 1650 gm. at birth. The average increment of increase from 6 to 9 months in Zeltner's series was 1.5 kg., and in ours, 1.8 and 1.3 and 2.1 and 1.0 kg., respectively.

Although both the height and weight curves steadily approached the 50th percentile as age increased, most of the babies had not yet reached or crossed this level by 24 months. This delay in attaining a normal average height and weight has previously been noted in premature infants of low birth weight.†

Periodic measurements of the circumferences of the head and chest revealed that the changes in these mensurations with increasing age throughout infancy were comparable in the three weight groups and that there was no essential difference between Group I and II infants within each weight category.

Perhaps more significant than physical measurements for assessing possible late effects of curtailed oxygen administration is in the motor and mental development of the infants in the two groups. Fifty children, 27 of them girls, were followed for one year or longer. This period was considered adequate to gain reliable impressions of developmental progress but too early for detailed tests such as the Stanford-Binet or Cattell infant intelligence test. These tests are planned when the children reach the age of 3 years.

The ages of attainment of the various levels of motor advancement are recorded in Table 8. There is no real difference in developmental speed between the Group I and Group II infants within each weight

TABLE 8.—*Average Motor Development of Infants for One Year or Longer Expressed in Months of Attainment*

Birth Weight, Gm.	Group	Observations*	Sex	Head Control	Hand Control	Rolls Both Ways	Sits Unaided	Creeps	Prehension	Pulls to Stand	Walks Support	Stands Alone	Walks Alone
1000 and below.....	I	4	1 M	4	6	7	11	11	6½	9	15	14	18
			3 F	3-5	6	5-9	9-13	11	6-7	7-9	13-17	10-17+	18
	II	1	1 F	4	6	8	10	11	10	11	12	15	18
1001-1361	I	16	10 M	5½	6	10	11	13	9	12	13	16	16
			6 F	3-12	5-12	6-12	7½-18+	10-18+	7-12	8-18+	10-18+	10-18+	12-19
	II	7	2 M	5	5	8½	10	11+	9	12	15	15	16
			5 F	3-5	4-6	7-11	8-18+	8-12+	8-12+	9-15	12-18	13-18+	14-18
1362-1650	I	14	7 M	4	5	8	10	11	10	11	13	15	16
			7 F	3-19	4-12	6-14+	7½-14	9-14	8-14	9-14	10-17+	12-21	13-22
	II	8	3 M	4	5	7	9	10	8	11	11	13	14
			5 F	3-5	4-6	6-9	8-22+	8-22+	6-9	9-22	9-22	12-22+	12-22+
Totals													
Average		50	23 M	4½	5½	8	10	11	9	11	13	15	16
Range			27 F	3-12	4-12	5-14+	7½-22+	8-22+	6-14	7-22	9-22	10-22+	12-22+

* The results are expressed so that for each Group the average age of attainment is on the first line and the range on the second line.

† Dunham,[8] pp. 83-87. Dann, M. and Levine, S. Z.: Unpublished data.

group, and the rate of motor development for all 50 babies, regardless of birth weight and duration of oxygen therapy, is comparable. The observed developmental schedule is in keeping with the findings of previous studies of prematures.[15]

If allowance is made for the degree of immaturity of the infants under consideration, the average age for attainment of the different motor levels is similar to that for full-term infants. In general the smallest babies were the most immature. Gestational ages of the 99 babies are present in Table 9. For the 50 infants whose developmental progress was recorded in Table 9, the average gestational ages were the same as for the total group of 99.

Although insufficient time has elapsed to certify the diagnosis of retardation, there are six infants whose mental or motor development or both appear abnormal. Three of them were in Group I, two were in Group II, and the sixth was originally assigned to Group II but did not come out of oxygen at the scheduled time and so was treated as a Group I baby. Their retarded development does not appear correlated with the absence of supplementary oxygen in the extrauterine environment, since there were more who received oxygen for a prolonged than for a brief period, and oxygen was administered to all for at least the first five days of life, probably the most crucial period if cerebral injury related to the complications of pregnancy and delivery has occurred. In at least three patients it is likely that injury to the central nervous system was sustained in utero or at birth, for there was bleeding in the third trimester of pregnancy, and in two labor was precipitate, while the third was extracted by midforceps because of prolapse of the cord. Their condition at birth was poor. It is of some interest that in an additional seven babies the neonatal period was equally stormy or even more hazardous; yet they appear to be developing normally. Two other retarded infants were identical twins with birth weights of 1010 and 1040 gm. One was assigned to Group I and his mate to Group II. Their behavior in the past two and one-half years has been both retarded and bizarre, and they are considered to have congenital brain defects. The sixth child with retardation, a Group I baby whose birth weight was 860 gm., has congenital hydrocephalus.

No other neurologic abnormalities have been found. An evaluation of speech, intellectual attainment, and social behavior has not been attempted, for the number of infants on whom observations were possible is too few to make the results meaningful. For the purposes of comparison of the long-term differences between infants who received supplementary oxygen for a short time as opposed to a more prolonged period, it can be said that no differences in these spheres are apparent in the two groups.

Incidental observations, probably unrelated to oxygen, on this group of infants include the presence of deafness in a girl who at birth weighed 1220 gm. She was born after an induced labor at 32 weeks' gestation to a mother with eclampsia who had two convulsions the day before delivery. The infant at birth was in poor condition, inactive, and with poor aeration of the lungs, retraction of the thoracic cage, and infrequent periods of apnea for the first two days. Nevertheless, when she was assigned to Group II of the oxygen study, she tolerated reduction of oxygen beginning at 48 hours and withdrawal from oxygen at five days. Because of the possibility of infection superimposed on atelectasis, she received for the first 11 days penicillin, 150,000 units, and streptomycin, 50 mg., twice daily, and again at 7 weeks because of signs suggestive of sepsis she was given penicillin, 200,000 units, and streptomycin, 100 gm., twice daily for 11 days. Whether the deafness is in any way related to the mother's eclampsia, to the administration of streptomycin for a total of 22 days to an immature infant, or to the early withdrawal from oxygen, or to none of these factors is unknown. Her subsequent growth and development have been normal except for her hearing disability.

As is true of small prematures in general, the incidence of strabismus, narrow and

elongated skulls, umbilical and indirect inguinal herniae, and hemangiomata was higher in these infants than in full-term babies. Two girls have cataracts. Dentition was slower than for full-term infants in that the usual appearance time of the first tooth was 8 to 10 months (range 6 to 14 + months), and several at 12 months were still toothless. The anterior fontanelle in more than half the babies was still patent at one year. No clinical evidence of rickets or scurvy was found; all infants received an adequate intake of vitamins A, D, and C.

CONCLUSIONS

From observations of the early course and subsequent progress during the first year or two of life of 99 premature infants of low birth weight, it is our impression that oxygen need not be administered routinely to small prematures. With the exception of some babies whose weights were below 1000 gm. and those with evidence of respiratory difficulty or intracranial damage in the first days of life, these babies tolerated early removal from oxygen without apparent ill effect. Aside from the important considerations regarding the possible harmful effect of oxygen in the causation of retrolental fibroplasia, a question under cooperative study currently at this and at other institutions, it would appear that from a practical standpoint there will result a great saving to premature nurseries in money, equipment, and time spent in nursing care, without detriment to the infants, if the custom of routine administration of oxygen is abandoned. When oxygen therapy is indicated, its use after the subsidence of symptoms need not be continued.

SUMMARY

Observations are presented on a group of 99 permature infants with birth weights of 1650 gm. and below who by a modified random sampling technique were kept in oxygen until a weight of 1600 gm. was attained (Group I, prolonged oxygen therapy) or were taken out of oxygen earlier, at 5, 10, or 17 days depending on the birth weight (Group II, curtailed oxygen therapy). For both groups, weaning from oxygen took place over a four-day period. The average time in oxygen was three to four times as long for Group I as for Group II infants. Oxygen concentrations, measured daily, were comparable for the two groups. Over half were in oxygen at concentrations of 40 to 50%, 19 at levels above 50%, and 26 at concentrations below 40%.

Except for five infants with weights less than 1000 gm. and two babies in poor condition at 48 hours of age at the time of scheduled oxygen reduction, all Group II infants tolerated removal from oxygen at the appointed time without difficulty. The subsequent development progress has been followed in 75 babies for a minimum of six months and in 50 for a minimum period of one year to as long as two and a half years.

TABLE 9.—*Gestational Ages of Infants*

Birth Weight, Gm.	Average	Range
1000 and below.....	27	26-30
1001-1361	31	28-36
1362-1650	32	28-40

The gain in weight and height and the rate of motor development of Group I and Group II infants was similar. There were no detectable late ill effects from the early termination of oxygen administration. It would seem that the administration of oxygen to premature infants of low birth weight as a routine procedure is not necessary. Definite conclusions must await similar follow-up studies on small premature infants exposed to lower concentrations of oxygen or to atmospheric oxygen from birth.

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Lead Poisoning in Children

Including Nine Cases Treated with Edathamil Calcium-Disodium

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During the 14-year period between 1939 and 1952, 20 cases of lead poisoning were diagnosed at the Children's Memorial Hospital. The greatest number in any one single year in this period was four. During the year 1953, the diagnosis of plumbism was substantiated by means of history and laboratory examination in 13 children. The apparent increase in the incidence of intoxication with materials containing lead prompted this report.

The 33 children in this report were all less than 5 years of age. The greatest incidence of occurrence was between 1 and 3 years of age and included 23 cases, or 70% of the total. Table 1 presents the age distribution of the 33 cases.

TABLE 1.—*Age Incidence of Thirty-three Cases of Lead Poisoning in Children*

Age, Yr.	No. Cases	Per Cent
0-1	1	3
1-2	14	43
2-3	9	27
3-4	7	21
4-5	2	6
5-6	0	0

The youngest patient in this series is a 10-month-old infant who had been nibbling upon a recently painted crib and furniture for three months. The oldest child is a girl aged 4½ years who had chewed on her bed.

Twenty of the patients are male, and 13, or 39%, are female.

Almost without exception these children come from families in the poorest economic groups, whose homes or apartments are in poor repair, often with paint peeling off the walls. Four of the 33 children were cared for by private physicians, and 29, or 88%, of the children were clinic patients. The homes of these patients were not situated in any one particular area of the city.

The seasonal incidence of the cases is in close agreement with that of other investigators, since 26 of the 33 patients, or 79%, were admitted to the hospital during the hot summer months of June, July, and August. No satisfactory explanation is available for this.[1] One school of thought questions the antirachitic effect of solar radiation during this period resulting in an increase of lead absorption from the intestine.

There were six deaths, or a total mortality of 18%.

The average duration of symptoms prior to hospital admission was 4.8 weeks, and ranged from 2 days to 6 months. Some children who were asymptomatic but who had a history of lead ingestion were admitted for observation because of a sibling hospitalized with lead intoxication.

The average duration of symptoms in those children who died was 2.4 weeks, with a range from 2 days to 8 weeks.

The symptomatic complaints elicited, in order of frequency, are seen in Table 2. The most common cause of lead poisoning in children is apparently the habit of chewing paint from cribs, toys, furniture, and woodwork, such as window sills, and the eating of painted plaster and fallen paint flakes. The tendency to put things in the mouth, though normal in the first year of life, is

Present address: U. S. Naval Hospital, Key West, Fla.

The EDTA, or Calcium Disodium Versenate, used was made available by Riker Laboratories, Inc., Los Angeles.

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considered abnormal if continued into the latter part of infancy and is referred to as pica, or perverted appetite. Pica is the usual forerunner of lead poisoning in children * and was elicited in the history of 94% of the cases and in all of those cases which occurred in 1953. The actual source of the paint was ascertained in 28 of the cases, or 85%.

Paint chips from window sills were incriminated in 13 cases, and paint and painted plaster from the walls in 8 cases. Ten children developed plumbism from chewing on painted cribs and furniture, but it is significant that 9 of these cases occurred prior to 1953. One would suspect that this represents the effect of legislation requiring paint manufacturers to label whether the paint is for indoor or outdoor use and the percentage of lead contained. This trend has also manifested itself in the toy industry, and the only two children who had painted toys as the source of their ingestion were among the first cases in the series. Four children gave no history of paint ingestion.

TABLE 2.—*Symptomatic Complaints of Lead Poisoning in Children in Order of Frequency*

Symptoms	No. Cases	Per Cent
Pica	31	94
Paint ingestion	28	85
Vomiting	23	70
Irritability	22	67
Constipation	21	64
Listlessness	20	61
Anorexia	18	55
Abdominal pain	15	45
Weight loss	15	45
Pallor	14	42
Convulsions	11	33
Urinary symptoms	9	27
Coma, stupor	8	24
Ataxia	7	21
Behavioral and mental changes	7	21
Tremors	6	18
Muscle weakness	6	18
Sleeping poorly	6	18

In the group of children seen in 1953, the actual source of the paint was examined in the homes † and specimens were collected and analyzed for their lead content by the Chemical Laboratory of the Chicago Board of Health. Of specimens obtained in nine of the homes, lead was present in amounts greater than a trace in seven and present as a trace in one. The window sills were found to have toxicologically significant quantities in all cases, painted wallpaper in one instance, and paint scrapings from a water tank in another. The trace of lead was present on the painted crib of our youngest patient. In no case was the source to be found in burned battery casings.[4]

The gastrointestinal symptoms of vomiting, constipation, anorexia, and cramping abdominal pains resulting in considerable weight loss in some of the patients were next in importance after pica and paint ingestion. Some children with no complaint of constipation were observed to have infrequent constipated stools during their hospital stay. In general, the vomiting usually occurred in the morning after breakfast.

The symptoms referable to irritation of the central nervous system rank in importance with those of the gastrointestinal system but in general are manifested later in the course of the illness. The complaints of drowsiness, lethargy, and fatigue are included with listlessness. Oftentimes, when pallor was not one of the complaints presented by the parents, it was noted by the examining physician. Those behavioral and mental changes noted were dullness, inactivity, withdrawal, refusal to play with other children, inattention, disobedience, and temper tantrums.

The physical examination was not remarkable in those children with no signs of central-nervous-system irritation. Twenty-six of the cases exhibited marked pallor. In 14 of the children, a Grade 2 or 3 musical-sounding systolic murmur was heard along the left sternal border, maximal at the third intercostal space. This was interpreted as functional in all cases and thought to be partially due to the anemia. The percentage was certainly no higher than that of functional cardiac murmurs heard in the total clinic population. The liver was palpable in

* References 2 and 3.

† Dr. Robert B. Mellins, U.S.P.H.S., helped in securing the specimens and obtaining their analyses.

30% of the cases, but when the age groups represented are considered, much significance cannot be ascribed to this finding. Hard fecal masses were palpable both in children with complaints of constipation and in those without. Stippling of the gum margins, due to deposits of lead sulfide in the capillaries, is dependent upon the release of sulfides from decaying organic matter in the mouth and is rarely found in young children.[5] This lead line was noted in only one patient, a 3½-year-old girl.

Signs of increased intracranial pressure, such as papilledema and Macewen's cracked-pot resonance, were present in those children who died. Tremor, ataxia, and motor weakness were present in several others.

Lead poisoning is a disease in which laboratory and roentgen examinations are often invaluable aids in diagnosis, but they must be correlated with the history of pica and definite ingestion of paint containing lead.

The red blood cell count of 15 children was less than 4,000,000. The counts ranged from 2,000,000 to 6,100,000, and the average was 4,100,000 red blood cells per cubic millimeter. These children have a hypochromic anemia. The average hemoglobin value was 8 gm. and ranged in value from 5.5 to 11.8 gm. Ninety-one per cent of the children had less than 10 gm. of hemoglobin. Basophilic stippling of the red blood cells was present in 94% of the cases at the time of admission to the hospital. Reticulocyte counts were abnormally high in almost all the children in which they were done. They averaged 4.6% in the 17 patients from whom they were measured. Stained smears on most of the cases showed the abnormal findings of polychromia, hypochromia, anisocytosis, poikilocytosis, microcytosis, and macrocytosis.

Renal tubular damage accounts for the albuminuria and glycosuria which may be found.[6] Albumin was found in the urine in slightly less than one-half of the patients, and glucose was demonstrated in 21% of the cases.

Urinary excretion of lead measured ‡ in 20 of the 33 patients was found to be significantly elevated in all. There was no correlation between the degree of severity of the symptoms of the illness and the quantity of lead excreted in the urine in 24 hours. The children who died in 1953 had levels of 0.215, 0.258, and 0.675 mg/liter/24 hours (the range of normal values varies between 0.001 and 0.08 mg/liter/24 hours). One child who had 0.762 mg/liter excretion for a 24-hour period was asymptomatic, but her sister, who had initial levels of 0.018, 0.004, and 0.175, had marked ataxia and tremors. This patient received two courses of therapy with edathamil calcium-disodium, and her urinary excretion rose during the second course to levels of 0.354, 0.419, and 0.666 mg/liter/24 hours. There was a tremendous increase in the quantity of lead excreted during edathamil calcium disodium therapy, with values greater than 100 times normal excretion being obtained.

During the second course of therapy, the values would often rise, lending support to the theory that lead is stored in depots other than the skeletal system.[7]

Porphyrinuria was present in six of the eight patients whose urines were analyzed. Porphyrins were not present consistently in the urine, however.

Levels of lead in the blood were analyzed in only two of the patients prior to 1953. The values obtained in those cases were 0.067 and 0.167 mg. per 100 cc., as compared with the normally accepted range of 0.03 to 0.06 mg. per 100 cc. Perhaps because of the apparent increase in the incidence of lead poisoning in children in the city of Chicago, as reflected by the 13 cases proved at the Children's Memorial Hospital, lead poisoning is to become a reportable disease in this city. In addition, facilities were made available for the determination of lead levels in the blood. Four samples were drawn in specially prepared syringes and needles and

‡ Urinary lead analyses were performed by the State of Illinois, Department of Public Health, Division of Laboratories (Alfred N. Setterlind, Chief Chemist).

TABLE 3.—*Blood and Spinal Fluid Chemistries and Urinary Lead Determinations Before and After Treatment with Edathamil Calcium-Disodium*

	Chemistries			C. S. F.			Urinary Lead Levels			
							Pretreatment		Post-treatment	
Pt.		Pre-treatment	Post-treatment		Pre-treatment	Post-treatment	Mg./L.	Vol.	Mg./L.	Vol.
BR	N. P. N.	28	23	Glue.	....	69	0.018	1020	0.419	620
	Prot.	6.8	7.4	Prot.	....	46.2	0.004	1050	0.666	570
	Alb.	4.2	4.8	Cl	....	707	0.175	640	0.354	650
	Glob.	2.6	2.6		....	....	.....	....	.....	....
	Ca	10.8	11.1		....	....	.....	....	0.281	300
	P	3.8	4.6		....	....	.....	....	.....	....
	P'tase	8.1	3.4		....	....	.....	....	.....	....
									0.6	1250
CH	N. P. N.	40	28		....	....	.....	....	5.0	575
	BUN.	21	....	Glue.	60	63	0.254	600	2.8	1275
	Creat.	1.1	....	Prot.	49.4	16.6	0.140	600	4.1	800
	Prot.	7.0	6.4	Cl	704	803	.....	....	2.1	775
	Alb.	5.1	4.5		....	....	.....	....	1.9	1025
	Glob.	1.9	1.9		....	....	.....	....	2.6	675
	Ca	10.6	9.8		....	....	.....	....	2.4	800
	P	3.8	4.4		....	....	.....	....	3.3	410
	P'tase	5.5	4.4		....	....	.....	....	2.2	375
							.....	....		
SG	N. P. N.	62	25	Glue.	44	70	0.115	450	4.0	1830
	BUN.	36	....	Prot.	33.5	34.3	1.2	1125	4.5	830
	Creat.	0.8	....	Cl	751	724	.....	....	2.4	425
	Prot.	6.7	6.2		....	....	.....	....	.....	....
	Alb.	4.8	4.3		....	....	.....	....	.....	....
	Glob.	1.9	1.9		....	....	.....	....	.....	....
	Ca	10.8	10.6		....	....	.....	....	.....	....
	P	3.9	5.7		....	....	.....	....	.....	....
	P'tase	....	11.4		....	....	.....	....	.....	....
FG	N. P. N.	37	....	Glue.	39	....	0.143	265	0.148	230
	Prot.	6.4	....	Prot.	13.1	....	.....	....	3.9	....
	Alb.	4.7	....		....	....	.....	....	2.3	....
	Glob.	1.7	....		....	....	.....	....	1.6	210
	Ca	12.2	....		....	....	.....	....	.....	....
	P	3.6	....		....	....	.....	....	.....	....
	P'tase	7.8	....		....	....	.....	....	.....	....
ES	N. P. N.	32	28	Glue.	60	77	0.100	....	0.3	1150
	Prot.	6.7	7.3	Prot.	141.1	24.4	.....	....	3.6	1075
	Alb.	4.0	4.6	Cl	795	713	.....	....	2.8	1275
	Glob.	2.7	2.7		....	....	.....	....	3.0	1210
	Ca	11.4	10.6		....	....	.....	....	2.9	1210
	P	3.3	4.3		....	....	.....	....	3.1	1325
	P'tase	....	6.8		....	....	.....	....	1.1	1425
							.....	....	1.5	1150
							.....	....	2.4	775
							.....	....	2.6	500
RH	N. P. N.	28	30	Glue.	40	66	.....	....	0.621	190
	Prot.	7.2	6.3	Prot.	60	27.1	.....	....	10.5	200
	Alb.	5.2	4.6	Cl	809	786	.....	....	5.4	920
	Glob.	2.0	1.7		....	....	.....	....	3.3	700
	Ca	10.2	10.2		....	....	.....	....	2.8	550
	P	5.7	4.0		....	....	.....	....	2.1	1300
	P'tase	2.7	3.5		....	....	.....	....	1.1	1300
							.....	....	2.9	750
							.....	....	1.6	325
							.....	....	2.8	550

placed in lead-free test tubes. The results showed 0.047, 0.056, 0.095, and 0.109 mg. per 100 cc. It is seen that the value of the blood determination lies in its use in screening patients with possible lead intoxication. Variables such as time of day the sample is drawn, ingestion of food, and pH of the blood determine the level of lead.

The increased density in the growing ends of the long bones on x-ray examination is

a cardinal sign of lead poisoning.[8] The x-ray changes were interpreted as significant and diagnostic of heavy-metal ingestion in 85% of the patients. The x-ray was interpreted as suggestive of lead poisoning in four patients and as negative in the 10-month-old infant mentioned earlier; yet these children had significant elevation of urinary levels of lead.

In addition to the dense lead line in the ends of the long bones, three children exhibited flecks of increased density throughout the large bowel on x-ray of the abdomen. These densities were interpreted as being paint chips from recent ingestion. Several of the children had more than one dense line at the ends of the long bones, which suggested an earlier period of ingestion of lead products.

Repeat roentgenograms taken as soon as four to six months following hospital discharge showed a decrease in the density of the lines previously seen, in addition to a widening of those lines. Complete disappearance was seen to occur in one year's time.

Lumbar punctures were performed, in the absence of papilledema, in 20 of the 33 cases. Abnormal dynamics or constituents of the cerebrospinal fluid were found in 16 instances. The spinal fluid pressure was elevated above 240 mm. of water in eight of nine patients in whom it was measured. Ten patients had 6 cells or less in the spinal fluid, and 10 had anywhere up to 128 cells. Eleven patients had more than 45 mg. per 100 cc. of protein in the C. S. F. Incidentally, in the patient with the greatest number of cells, i. e., 128, the protein was only 36.1 mg. per 100 cc.

The admitting diagnosis to the hospital was lead poisoning in 57% of the cases. Renal pathology was suspected in three cases because of symptoms of polyuria, oliguria, anuria, and the presence of dark reddish-brown urine. Brain abscess, tuberculous meningitis, and convulsive disorder were considered in another three cases; one child was operated upon for a brain tumor.[9] Gastritis or pernicious vomiting was the reason for hospitalization in three cases. Two children were suspected of having diabetes mellitus because of the presence of reducing substance in the urine and symptoms of polyuria and polydipsia. Two children were admitted because of severe anemia. In only two of the patients was there a complicating upper respiratory infection present. This point is mentioned because it is known that any marked change in the acid-base equilibrium of the blood by disease tends to mobilize the stored lead and place it back into circulation.

One child was readmitted because of abdominal pain, which was relieved by calcium gluconate. This was thought to be due to lead colic for this reason.

The average duration of the hospitalization was three weeks and ranged from one day to nine weeks. Three patients died within the first 24 hours of hospitalization.

Electroencephalograms were taken during the course of the acute illness in eight patients and sometime after hospital discharge in four others. Wake, drowsy, light and deep sleep, and arousal records were taken from bilaterally placed frontal, temporal, anterior temporal, parietal, and occipital leads. The record was normal in only 3 of the 12 children. A common pattern was seen in eight cases, with most of them showing a generalized reduction in the amplitude of the waking record, often accompanied by considerable 20/sec. activity. An abnormal amount of low voltage fast (25/sec.) activity was present in all leads in the waking, drowsy, light and deep-sleep records. Reduction in the amount of slow wave activity of drowsiness and light sleep was reported frequently.

These changes are not specific but are indicative of a generalized irritative phenomenon and central nervous system deterioration. They have not been previously reported in a series of lead poisoning cases.

The treatment of lead poisoning has undergone a dramatic change by the addition of edathamil calcium-disodium to the armamentarium. This substance is a nontoxic agent which can mobilize lead, form a stable compound with it, and then rather promptly be

excreted in the urine. The edathamil calcium-disodium is given by the intravenous route as a 3% solution or less. The maximum dose is 0.5 gm/30 lb. (13.6 kg.)/hour, 1.0 gm/30 lb/day, 5.0 to 7.0 gm/30 lb/course, with seven days rest between courses. Edathamil calcium-disodium was used in nine patients in 1953, three of whom died within the first 36 hours of hospitalization. In these cases the treatment was aimed primarily at reducing the cerebral edema by means of magnesium sulfate by proctoclysis, hypertonic dextrose intravenously, phenobarbital, and, in one instance, by a craniotomy and subtentorial decompression. When the dura mater was exposed, there was no pulsation of the brain. As the dura was incised, pulsations were visible.

In the other six cases, there was marked improvement of the symptoms of central nervous system irritability, as well as the gastrointestinal and urinary symptoms. Elevated spinal fluid cell counts and proteins returned to normal values after two courses of therapy.

No adverse effect of the edathamil calcium-disodium therapy was encountered. These children were followed by serial blood cell counts, urinalyses, and blood chemistry determinations. The nonprotein nitrogen, serum proteins, calcium, phosphorus, sodium, potassium, chlorides, pH, and carbon dioxide content were not altered adversely in any of the cases.

In only one case was a direct sensitivity to the preparation suspected. This child developed a fever and maculopapular eruption 11 days after a 5-day course of therapy was initiated. Giant urticaria was present the following day. The eruption persisted four days after antihistamines were started. A second course of therapy was not given, but 0.1 cc. of a 1:10 dilution of the edathamil calcium-disodium solution was given as an intradermal test, and no reaction developed at the skin site.

Therapy which had been utilized in the past included vitamins D and C in 27 children, iron in 22, and calcium in 10. This latter was given with phosphorus in only three cases. Sodium citrate was used in four cases. Supportive therapy of I. V. fluids for severe persistent vomiting and blood transfusion for pronounced anemia was given. During the years 1950-1951, dimercaprol (BAL) was successfully used in three cases.

Byers and Lord[10] reported on the late effects of mild lead poisoning on mental development. They performed serial psychometric testing in grade school. We were able to do psychometric examinations on 10 of the children at variable lengths of time following their hospitalization, partially to afford a baseline value for comparison with later performances. The developmental data on the children in this series do not support the view that pica was present because of mental defect, since in all cases the children had normal birth and developmental histories prior to ingestion of paint.

The basic pathological changes in lead encephalopathy are edema, punctate hemorrhages, gliosis, and focal areas of necrosis throughout the brain. These changes are undeniably irreversible. Lead deposited in the brain may directly injure or kill nerve cells. In one of the cases the basal ganglia in particular were seen to have pale swollen vacuolated parenchymatous brain tissue. The blood vessels were congested. A few small perivascular hemorrhages and a few small petechial hemorrhages were seen. Neurones everywhere showed toxic changes, especially in the basal ganglia where they were undergoing chromatolysis. The lead analysis of the tissues in this case was as follows: kidney, 0.39 mg./100 gm. tissue; liver, 4.94 mg./100 gm., and bone, 17.6 mg./100 gm.; these are considerably higher than values found in children of the same age dying from other causes.[11]

An invaluable aid in confirming the diagnosis has been the presence of acid-fast intranuclear inclusion bodies in the kidney and liver, as described by Blackman.§

The prognosis in lead poisoning as well as the more severe encephalopathy in children must be guarded. The high mortality rate, as well as the incidence of severe life-long

§ References 12 and 13.

residual nervous system injury, has been noted by many investigators. The mental development of even the less severe cases may be seriously impaired.

SUMMARY AND CONCLUSIONS

The age, sex, economic, and seasonal incidence of lead poisoning in children in a series of 33 cases is presented.

The sources of the ingested paint are enumerated.

The symptoms are described, and the important role played by pica is emphasized.

Typical laboratory and roentgen findings are discussed, with report of electroencephalographic studies.

The differential diagnosis is discussed.

Excellent results were obtained in six of the nine patients treated with edathamil calcium-disodium. The three patients who died presented the picture of severe encephalopathy.

There is a high mortality and in general a poor prognosis in lead intoxication in children.

An explanation for the increased incidence of cases in 1953 may be the added interest in the problem.

Lead poisoning will soon be a reportable disease in Chicago.

The Social Service Department, particularly Miss Jean Van Velsor, facilitated adequate follow-up studies on the children.

Dr. Richard M. Elghammer, Dr. Donald W. Jackson, and Dr. Robert W. Thomas cooperated in this study.

Electroencephalograms were taken by Miss I. Collins, R. N., and interpreted by Dr. William C. Wilson, electroencephalographer, Children's Memorial Hospital.

Dr. John A. Bigler, Chief of Staff of the Children's Memorial Hospital and Professor of Pediatrics and Head of the Department, Northwestern University Medical School, gave advice and encouragement.

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Pictorial and Graphic Analysis of the Body Build of One Boy

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A commonplace of life is than man, like other living organisms, changes in both size and shape throughout his life cycle. In the last century the basic patterns of change in size for man en masse have been well traced by means of the statistical parameters for many dimensions of the body and its parts. A beginning has been made on the over-all pattern of change in shape by a combination of pictorial and graphic methods. Continuous studies on single persons are still few and limited to only parts of the life cycle, not from unawareness of the value of total life cycle studies, but because of the formidable task of obtaining the basic data.

This study is a presentation of new combinations of existing pictorial and graphic techniques in order to visualize the changes in size and form of one boy from 4 to 19 years of age. It is essentially an extension to the study of individual children of the iconometrographic technique used so effectively by Scammon [1] and his students [2] for demonstrating growth of anatomical structures. The text, as in an atlas, is only a guide to how to look at the graphs and pictures. The historical background is limited to indicating a few key references for each method.

The work is exploratory in preparation for the analysis of patterns of individual growth for approximately 100 children whose records will be completed from birth to at least 20 years of age within the next five years.

NATURE AND SOURCE OF DATA

The basic data are from three types of observations included in the longitudinal records on growth being collected at the Child Research Council. The first are photographs of anterior, posterior, and lateral views of the body taken to one-tenth actual height once yearly and usually, but not always, on the birth-date visit. They were originally taken as a record of natural and not instructed posture, so that exact positioning is not as well standardized as is object film distance. However, after about 6 years of age most children are fairly consistent in the position they take. Second are the 14 standard anthropometric measurements [3] of external dimensions from a list of 24 that have been maintained with reasonable uniformity from birth to maturity by five successive workers. Tentative percentile standards [4] have been set up for each dimension and age, using ordinary cross-sectional technique. They are based on from 17 to 45 boys at each age up to 18 years, with the same boys included at many ages. The projections of curves from 18 to 22 years are only rough approximations, being based on about ten boys per year. In about five years sufficient data will have accumulated to establish longitudinal * percentile standards based on measurements of the same children from birth to 20 years of age. At that time a detailed report on the methods of the measuring, summary

From the Child Research Council and the University of Colorado School of Medicine.

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* References 5 and 6.

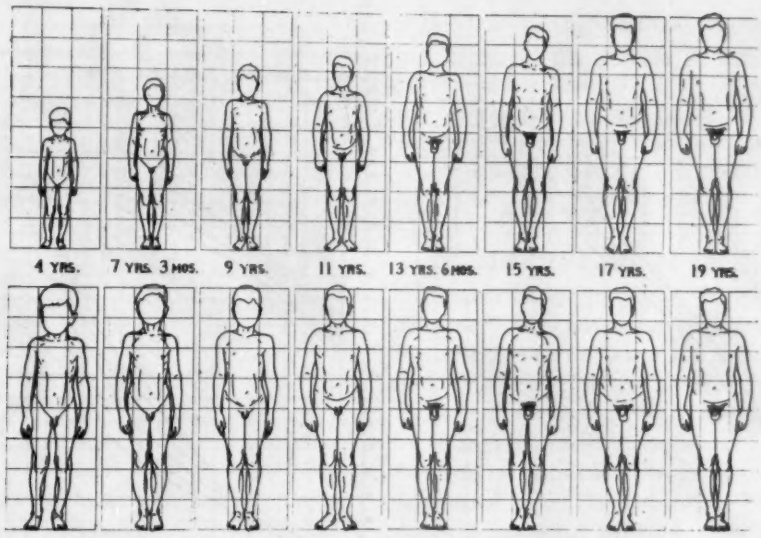

Fig. 1.—Outline tracings of photographs of one boy for eight ages from 4 to 19 years, first according to actual height and second to constant height. The grid is one-eighth of the constant height.

tables, and new percentiles will be published. Third are the x-ray films, taken with well-standardized technique for 20 years. Measurements and percentile standards of the lengths and widths of the long bones of the upper and lower extremities have been made by Dr. Maresh [7] from these films.

PICTORIAL SERIATION

The dual problem of analyzing size and form is illustrated in Figure 1 by two simple devices: First, seriation of outline tracings of anterior photographs of this boy for eight ages, and, second, enlargement of each one to common height, a process labelled iconometrography by Wilmer and Scammon.[2] The second series makes apparent at a glance the well-known decrease with age in relative head size and the increase of relative leg length until puberty with a very slight decrease after puberty. The common expression of a "longlegged adolescent" indicates the general awareness of this change which, of course, results from the earlier spurt in leg length followed by the continued growth of spine after the epiphyses of the long bones are closed. A little more careful scrutiny brings out the marked widening of this boy's hips by 11 years and a later widening of his shoulders and especially his chest after puberty. Also, he appears thin at the first two ages, then progressively heavier except at 15 years, when he becomes temporarily slimmer. This impression can be evaluated better by the comparison of the measurements of his height and weight with those of other boys in the next section.

PERCENTILES OF HEIGHT, WEIGHT, AND PONDERAL INDEX

The first questions asked in evaluating a person's physique are "How tall is he?" "How much does he weigh?" and "How heavy is he for his height?" These are readily answered by plotting his height, weight, and weight-height ratio (the ponderal index of Rohrer, cited by Baldwin [8]) on their respective percentile standards of central trend and variation with age in Figures 2, 3, and 4.

Inspection of Figure 2 shows that this boy's height made two major shifts from the 50th to the 90th percentile and back again to the 50th, a not unusual pattern in our series. In other words, he started and ended average in height, but for a short time in infancy and for most of his middle childhood he was moderately tall. His weight in Figure

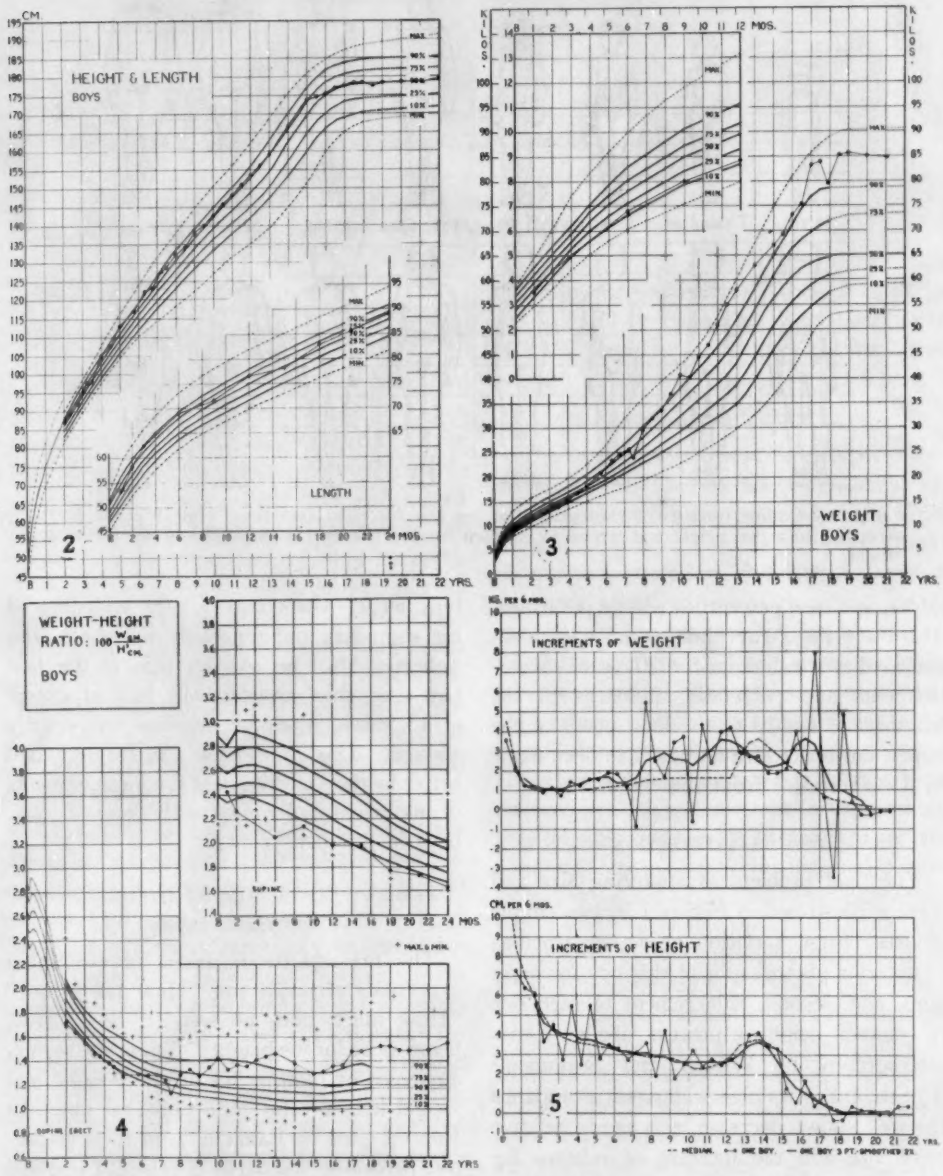

Fig. 2.—The height of one boy plotted on the smoothed percentiles of height for age for Child Research Council boys. Length is measured with child lying down.

Fig. 3.—The weight of one boy plotted on the smoothed percentiles of weight for age for Child Research Council boys.

Fig. 4.—The weight-height ratio (ponderal index of Rohrer) of one boy plotted on smoothed percentiles of those for age for Child Research Council boys.

Fig. 5.—Unsmoothed and twice-smoothed six-month increments of both weight and height of one boy plotted on the six-month increment curves of the median (50th percentile) of weight and height, respectively.

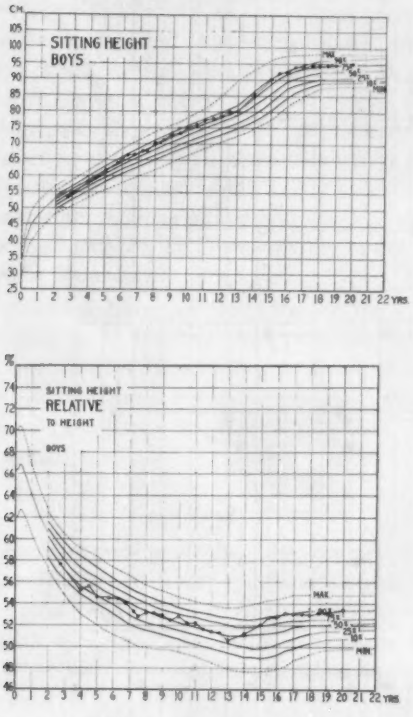

Fig. 6.—Sitting height in centimeters and in per cent of total height of one boy plotted on the respective smoothed percentiles for Child Research Council boys.

3 shows a strikingly different pattern, making, after 4 years of age, a staggered but persistent rise from the 10th to well above the 90th percentile. His ponderal index in Figure 4 makes a parallel spectacular shift which substantiates the impression gained from the photographic outlines.

INCREMENTS OF HEIGHT AND WEIGHT

Another basic question is "How fast is he growing?" This can be answered by plotting the increments for each six months [9] for both height and weight on the six-month increment curves of the 50th percentiles (medians) of each dimension in Figure 5. In order to minimize the effect of the experimental error in measuring [10] and the daily physiological variation in both height and weight, the fluctuating trends were smoothed by two applications of three-point smoothing. The reliability of these smoothed curves will be evaluated in a later study. During childhood his increment of height intertwined with that of the median, tending to be slightly above it. His circumpuberal spurt occurred at the same time but was markedly below that of the median. In short, he tended to grow slightly faster than the

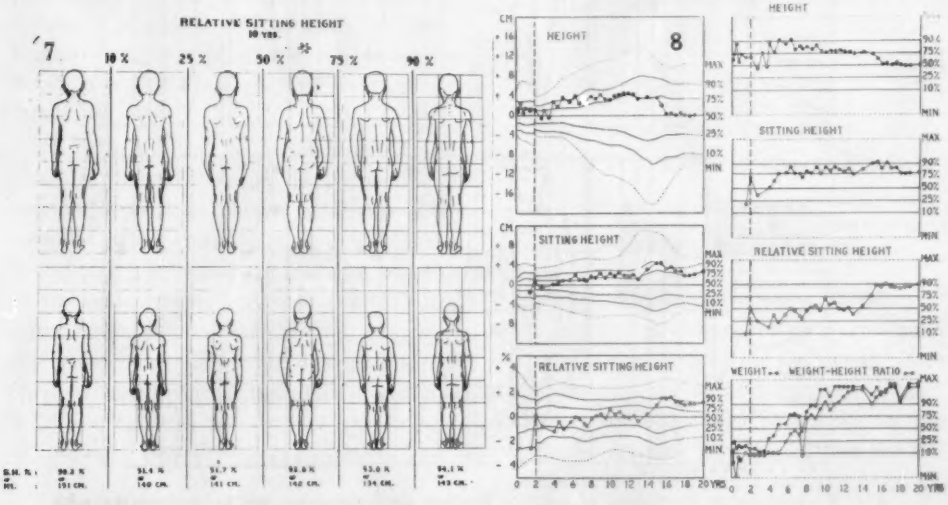

Fig. 7.—Upper panel, outline drawings of posterior photographs of six 10-year-old boys, one for each percentile zone of relative sitting height, with this boy indicated by asterisk. Lower panel, same series to actual height against a frame of average adult height.

Fig. 8.—Figures 2 and 6 reduced to semirectilinearity in left-hand panel and Figures 2, 6, 3, and 4 to rectilinearity in right-hand panel.

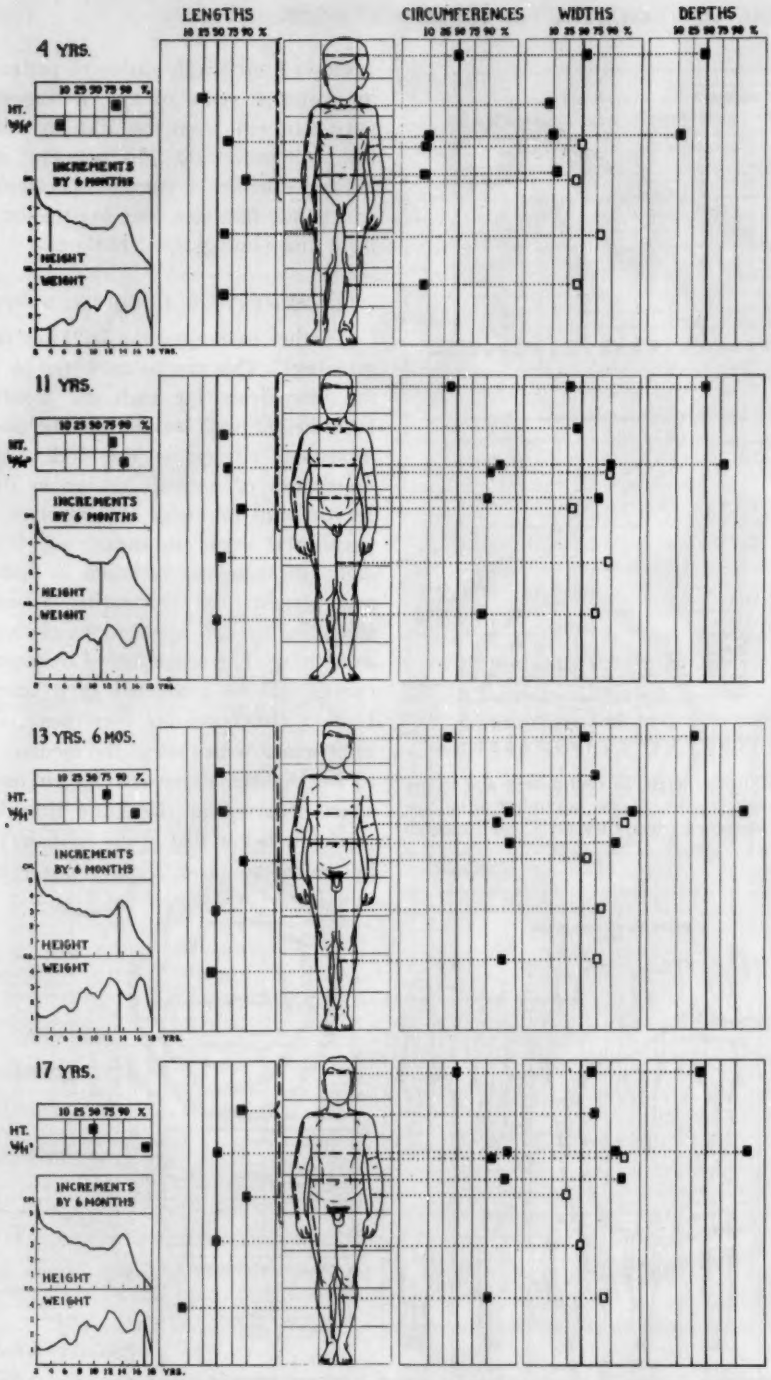

Fig. 9.—Rectilinear percentiles of relative lengths, circumferences, widths, and depths with respect to height of one boy, combined with photographic outlines for four ages. The open squares indicate position of widths of bones from x-ray films and the solid ones all other dimensions. They are joined by dotted guide lines to heavy broken lines on the photographic outline to indicate the part measured. In the left-hand panels, his percentile position in height and in weight for height are given and his progress on the increments of height and weight indicated by a vertical line.

group in childhood, but his circumpuberal spurt was less and of shorter duration than that of the median. This course fits with his shifting position in percentiles of height. His progressive heaviness, with its temporary reduction at puberty, is clearly shown by the high fluctuating level of his weight increment curve after 4 years of age and the concomitance of one of its dips with the spurt in height increment.

A better frame of reference for the rate of growth of one boy than the increments of the median is probably a series of individual increment curves.[5] These again await the accumulation of more completed individual records.

PROPORTIONATE PARTS

By the middle of the 19th century the proportions that linear dimensions made of the total height were in common use to describe age, sex, and racial differences in average body form by the artist and anthropologist.[11]

To illustrate the extension of this principle to the individual as compared with the group, this boy's sitting height both in actual centimeters and in per cent of total height are plotted on the respective percentile trends for age in Figure 6. On the whole his sitting height is long for his age, but for his age and height it is at first short, then average, and finally very long.

The effectiveness of holding height constant to show differences in proportion in contrast to size is shown in Figure 7 by combining the percentile position of the relative sitting height and the pictorial seriation of posterior tracings to both constant and actual height for 10-year-old boys. Considerable experimentation with this method applied to other characteristics indicates that it will be a useful tool in building an atlas on physical growth.

SEMIRECTILINEAR AND RECTILINEAR PERCENTILES AND PICTORIAL SERIATION

In order to visualize the trends of several dimensions at once, Dr. Maresh and I have reduced the curvilinear percentile standards for all dimensions first to semirectilinearity and second to total rectilinearity as shown in Figure 8. In the first, the 50th percentile is plotted as zero and the other percentiles as actual differences from it. Then the measurements for a given person are likewise plotted as their difference from the 50th percentile. In the second, all percentiles are reduced to parallel equidistant straight lines with the minimum and maximum lines

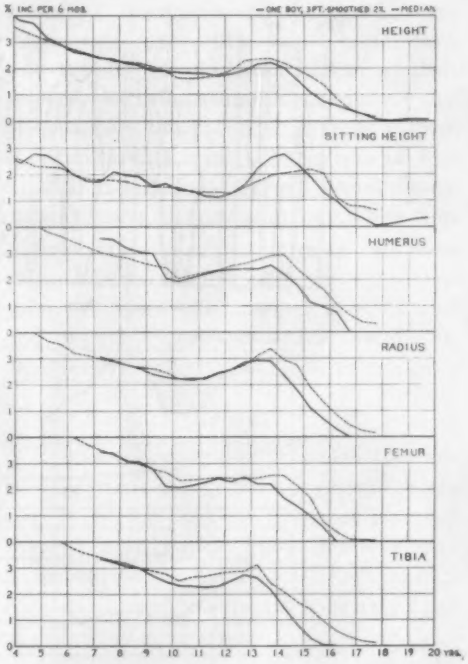
% INC. PER 6 MOS.
— ONE BOY, 3PT.-SMOOTHED 2%, — MEDIAN
HEIGHT
SITTING HEIGHT
HUMERUS
RADIUS
FEMUR
TIBIA
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 YRS.

Fig. 10.—Percentage increments of several lengths of one boy plotted on the percentage increment curves of the corresponding medians.

double distance from the 10th and 90th percentile, as if this were a probable error scale of ±4 probable errors from the mean.[12] Both methods bring the shift in position of each dimension into sharper focus than on the curvilinear trends. The former has the advantage of keeping in view the unit of measurement and its variation with age.[13] The latter has the great advantage that one grid can be used for more than one dimension, and 8 to 10 grids can be placed on one chart.

The rectilinear percentile grid has become a major working tool in analyzing body form; but when more than 10 dimensions are to be considered, they are too cumbersome for clear exposition. This has been overcome by a combination of pictorial and graphic methods for four sample ages, as shown in Figure 9. In the left-hand panels for each age are summarized this boy's position in percentile standards of height and ponderal index and on his increment curves of height and weight. The percentile positions of 18 other dimensions, reduced to per cent of height, are indicated by open squares for widths of bones from x-rays and solid ones for other dimensions, in four panels according to type of dimension.

Looking at the panels for lengths through the four ages, it becomes apparent that this boy has changed progressively from a short-trunked little boy with both femur and tibia slightly longer than average, to a very long-trunked young man with a femur of average length and a very short tibia. Over the same

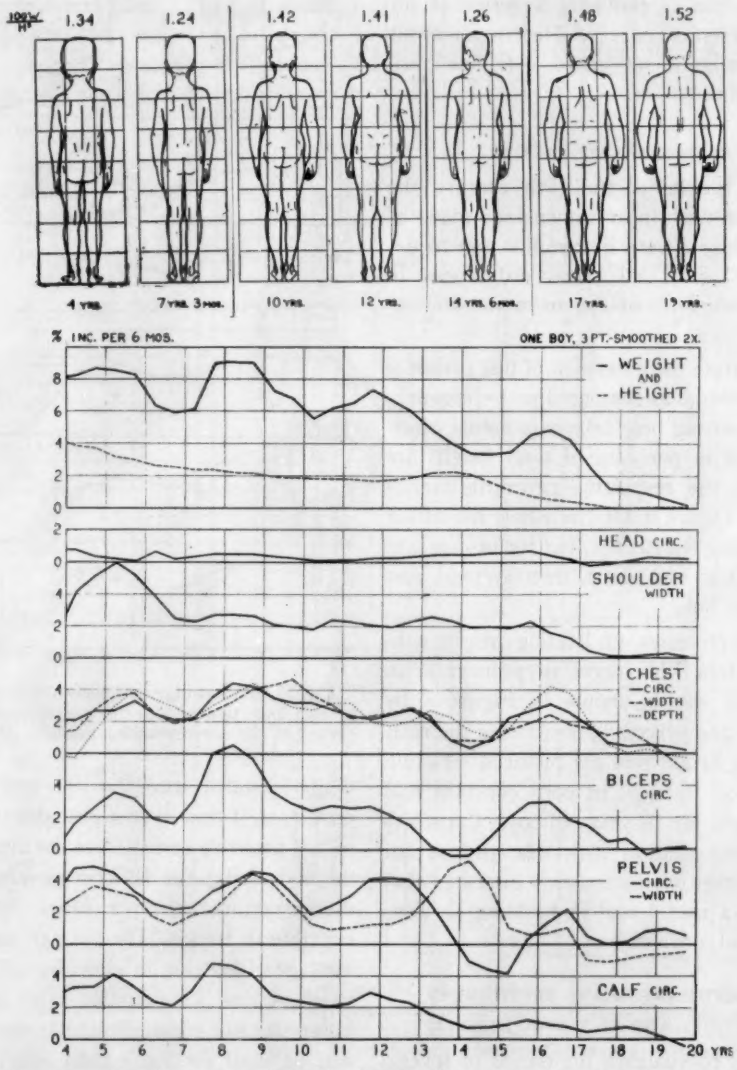

Fig. 11.—Percentage increment curves of height, weight, circumferences, widths, and depths of one boy, combined with selected posterior photographic tracings.

time period, his arm bones have remained long. The panels for circumferences and diameters show that his trunk not only becomes longer, but wider and deeper. His shoulders, however, while wide for a boy of his age, are relatively narrow for his torso. Some of his gain in percentile rank in weight appears to be due to increase in relative width of bone, as well as increase in soft tissue. And, finally, his head has remained of average size for his age and height.

PERCENTAGE INCREMENTS

Changes in body form with age are brought about by differing rates of growth of the skeletal segments, the enclosed viscera, and the overlying muscle and fat. This boy's change in position in the group indicates that besides the basic age changes, his differential rates are in some way deviant from those of other boys. The true specific rate [14] of each dimension can be approximated by the relative six-month increments in the form of

$$\% \text{ inc. per 6 mo.} = \frac{Y_2 - Y_1}{\left(\frac{Y_2 + Y_1}{2}\right)} 100$$

when Y_1 is the measurement of the dimension at the beginning of the six-months' period and Y_2 the value at the end. As with absolute increments, the excessive fluctuations need to be stabilized by three-point smoothing twice.

When this boy's smoothed percentage increments of lengths are plotted on those of the respective medians in Figure 10, the mechanism for his deviation in linear proportions becomes apparent. His basic patterns are the same as those of the medians, but the circumpuberal spurts are all early except for that of the radius. The maximum increment of the sitting height is markedly higher and those of the long bones, especially of the tibia, are lower and of shorter duration than those of the medians.

The labor of extending this comparison to relative increments of the median for each lateral dimension does not seem justified until more data have accumulated. However, some insight into the possibilities of this method can be gained by plotting this boy's percentage increments of weight, height, circumferences, widths, and depths under a series of his posterior photographic outlines in Figure 11. The four maxima of the percentage increments of weight are closely followed by his ponderal index, his appearance, and, with a few striking exceptions, the percentage increments of his circumferences, widths, and depths. With the circumpuberal spurt in height, the iliac crest widens while the circumference actually decreases. The biceps seem to take excessive part in the 8-year-old maximum and the pelvis in the 12-year-old one, and the calf does not enter into the 16-year-old spurt. After an early marked spurt, the shoulders maintain a uniform slightly low rate and drop off without a circumpuberal spurt. Comparison of Figures 10 and 11 show that all lateral dimensions continue to grow after long bones stop.

Just how closely variations in these smoothed-increment curves can be interpreted to mean real changes in rates over and beyond experimental error awaits the analyses of more records.

SUMMARY

A series of charts is presented to show how one boy's change in body form with age can be traced both in terms of his own changes in proportion due to different rates of growth of the parts of his body and in comparison with the proportions and rates of growth of other boys.

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Studies of Duodenal Fluid in Nutritional Disorders

Alkaline Phosphatase

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The assay of duodenal fluid for the activity of the digestive pancreatic enzymes is a well-established procedure in the study of nutritional disorders in early life. In mucoviscidosis with complete pancreatic insufficiency lipase, amylase, protease, chymotrypsin, and carboxypeptidase are absent or markedly reduced. In some instances of mucoviscidosis one may obtain a partial or selective reduction of enzyme activity.[1] In idiopathic celiac disease, as in a great variety of other nutritional disorders, the activity of pancreatic enzymes in duodenal fluid is normal.* However, deficiencies of pancreatic amylase in celiac disease [2] and of all the digestive enzymes in some patients with severe malnutrition and in kwashiorkor [4] have been claimed. Although alkaline phosphatase is not a "digestive" enzyme, it is also secreted by the pancreas. Its activity in the duodenal contents represents, in addition, the contribution from the liver and of the intestinal mucosa. The purpose of this report is to present the values for alkaline phosphatase activity in duodenal fluid obtained from infants and children with a wide variety of nutritional disorders.

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* References 1 and 2.

METHODS

The patients selected for study were grouped as follows: complete pancreatic insufficiency, partial pancreatic insufficiency, idiopathic celiac disease, unclassified nutritional disturbances, a miscellaneous group of sick children, and a control group of apparently healthy children. In addition, a small number of adults was included. Except for this last group, the age range of the patients varied from 1 month to 10 years, with the majority between 5 months and 2½ years.

The duodenal fluid was obtained after an eight-hour fast and was examined for the activity of amylase, lipase, protease, and carboxypeptidase; bile content; pH; volume, and viscosity.[1] The bile concentration was measured colorimetrically by using the duodenal fluid diluted 1/100 with distilled water, with filter 420 in the Klett colorimeter. The scale readings were recorded as a measure of bile concentration. The fasting values fell between 20 and 150. The highest values recorded following oil stimulation with resultant emptying of the gall bladder were in the vicinity of 700 to 800. The alkaline phosphatase was measured by a modification of the King-Armstrong method.[5] A 1/20 dilution of duodenal fluid was employed, using 1 ml. with 10 ml. buffer-substrate, at pH of 9.3. The incubation was carried out at 38 C for 60 minutes. Activity is expressed in milligrams of phenol liberated by 100 ml. of duodenal fluid. Acid phosphatase was also measured, using 1 ml. of duodenal fluid, diluted 1/20, in 10 ml. of buffer-substrate at pH 4.9.

In many instances the digestive enzymes as well as the phosphatase in the duodenal fluid were studied after stimulation of the pancreas and gall bladder by the intraduodenal instillation of olive oil. The amount of oil administered varied from 5 ml. to 15 ml., the larger amount being used in older children.

RESULTS

The alkaline phosphatase activity of duodenal fluid obtained from 120 persons in the fasting state is shown in Table 1. There appears to be considerable variation in the phosphatase activity of duodenal fluid in each of the groups of patients studied. In patients with pancreatic insufficiency one notes a con-

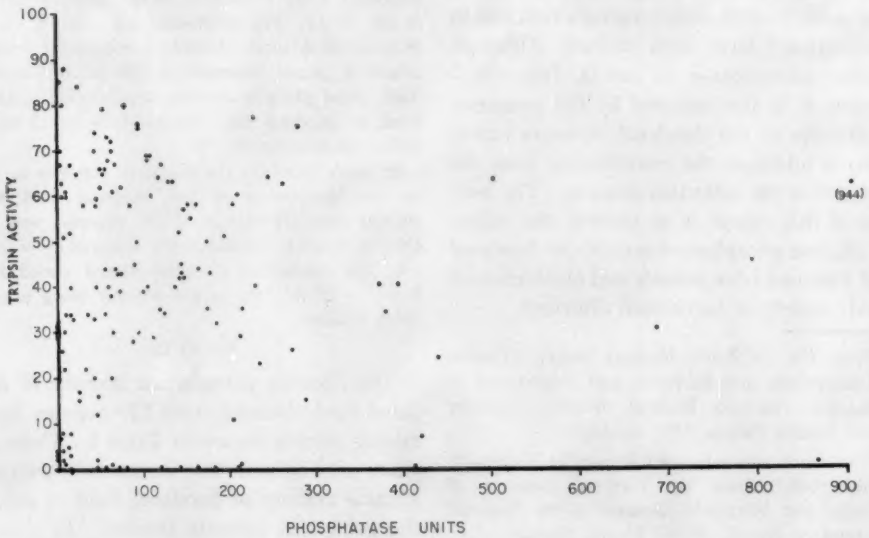
TABLE 1.—*Fasting Values of Alkaline Phosphatase in Duodenal Fluid*

Diagnosis	Patients, No. (120)	Mg. Phenol Liberated/100 Ml.
Healthy children	17	11, 16, 44, 60, 87, 94, 103, 114, 153, 183, 211, 232, 266, 378, 468, 539, 890
Mucoviscidosis		
Complete pancreatic insufficiency	35	0, 0, 0, 5, 6, 6, 6, 14, 15, 16, 19, 34, 48, 52, 53, 62, 70, 72, 73, 111, 111, 147, 165, 186, 208, 231, 243, 256, 268, 296, 350, 384, 413, 810, 868
Partial pancreatic insufficiency	10	9, 12, 24, 56, 66, 96, 147, 174, 536, 630
Celiac disease, idiopathic	6	41, 73, 108, 136, 216, 408
Nutritional disorders	17	31, 48, 50, 56, 62, 68, 71, 94, 99, 108, 110, 170, 179, 214, 228, 287, 440
Biliary atresia	5	19, 107, 289, 331, 944
Miscellaneous diseases	21	3, 11, 17, 21, 23, 34, 51, 53, 67, 70, 87, 110, 110, 130, 142, 143, 149, 270, 280, 323, 505
Adults (miscellaneous diseases)	9	0, 5, 9, 14, 44, 62, 84, 165, 186

siderable variation of phosphatase activity, with many low values and a few very high ones. In 19 of the 35 patients with complete pancreatic insufficiency the alkaline phosphatase was less than 80 units. A similar spread of activity is noted in patients with partial pancreatic insufficiency, in which the concentration of the various digestive enzymes may be moderately to markedly reduced, and not necessarily to a parallel degree.

The relationship of the alkaline phosphatase to the digestive enzymes was determined by comparing the activities of each of the digestive enzymes with the activity of alkaline phosphatase. The Figure shows the lack of correlation between protease activity, as measured by a turbidimetric procedure,[6] and alkaline phosphatase. The same results were obtained when the activity of amylase, lipase, and carboxypeptidase was compared with that of alkaline phosphatase. When each of the groups of patients are analyzed separately we note the same dissociation.

The relationship of bile concentration to alkaline phosphatase of the duodenal fluid is shown in Table 2. No correlation can be noted among the various groups of patients. However, there are a number of instances in which both the concentration of bile and the alkaline phosphatase are low. This relationship is noted with greater frequency in the patients with pancreatic insufficiency. On



Lack of correlation between trypsin activity and alkaline phosphatase.

TABLE 2.—*Relationship of Alkaline Phosphatase to Bile Concentration in Duodenal Fluid in Fasting State*

Healthy Children (10)*		Complete Pancreatic Insufficiency (29)		Partial Pancreatic Insufficiency (11)		Celiac Disease (4)		Nutritional Disorders (16)		Biliary Atresia (5)		Miscellaneous Diseases (16)		Adults (Misc. Dis.) (12)	
P†	B†	P	B	P	B	P	B	P	B	P	B	P	B	P	B
11	112	0	7	9	28	41	15	31	0	19	7	3	24	0	12
60	16	0	72	12	50	106	13	48	7	107	0	17	15	2	43
87	7	5	0	19	9	136	15	50	15	289	5	21	3	9	15
87	245	6	9	24	34	403	73	50	15	331	5	39	80	9	66
94	21	6	9	56	30	..	..	62	42	944	0	51	90	14	10
114	27	6	49	62	30	..	..	68	9	..	..	58	9	25	17
153	16	14	3	66	32	..	..	71	108	..	..	67	500	30	26
232	40	15	25	96	34	..	..	94	29	..	..	70	6	44	39
378	103	16	24	147	50	..	..	99	70	..	..	110	8	62	22
890	95	19	65	208	47	..	..	108	50	..	..	110	28	84	53
..	..	34	50	536	90	..	..	110	16	..	..	130	48	165	70
..	..	48	30	..	..	..	..	170	52	..	..	142	43	180	80
..	..	52	30	..	..	..	..	179	52	..	..	143	15	..	..
..	..	53	55	..	..	..	..	228	90	..	..	149	74	..	..
..	..	70	102	..	..	..	..	287	99	..	..	280	34	..	..
..	..	72	27	..	..	..	..	440	16	..	..	323	36	..	..
..	..	73	43	..	..	..	..	..	..	..	..	..	..	..	..
..	..	111	25	..	..	..	..	..	..	..	..	..	..	..	..
..	..	111	108	..	..	..	..	..	..	..	..	..	..	..	..
..	..	147	24	..	..	..	..	..	..	..	..	..	..	..	..
..	..	165	36	..	..	..	..	..	..	..	..	..	..	..	..
..	..	186	88	..	..	..	..	..	..	..	..	..	..	..	..
..	..	231	39	..	..	..	..	..	..	..	..	..	..	..	..
..	..	268	43	..	..	..	..	..	..	..	..	..	..	..	..
..	..	350	18	..	..	..	..	..	..	..	..	..	..	..	..
..	..	384	93	..	..	..	..	..	..	..	..	..	..	..	..
..	..	413	50	..	..	..	..	..	..	..	..	..	..	..	..
..	..	810	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	868	..	..	..	..	..	..	..	..	..	..	..	..	..

* Number of patients is given in parentheses.
† P, alkaline phosphatase; B, bile concentration.

TABLE 3.—*Relationship of Bile to Alkaline Phosphatase in Duodenal Fluid Before and After Intraduodenal Instillation of Oil* *

Healthy Children				Complete Pancreatic Insufficiency				Partial Pancreatic Insufficiency				Celiac Disease				Misc. Diseases			
Case	Sample	P†	B†	Case	Sample	P	B	Case	Sample	P	B	Case	Sample	P	B	Case	Sample	P	B
1	1	11	112	1	1	350	39	1	1	66	32	1	1	41	15	1	1	..	58
	2	..	..		2	..	..		2	62	57		2	90	24		2	10	62
	3	..	395		3	..	..		3	..	..		3	18	60		3	..	..
	4	0	20		4	310	208		4	146	115		4	57	24		4	99	54
	5	18	91		5	225	117		5	147	95		5	48	24		5	214	110
	6	16	100		6	198	90		6	128	50		6	57	24		6	195	87
2	1	60	16	2	1	72	55	2	1	9	28	2	1	108	13	2	1	149	74
	2	37	46		2	8	18		2	..	..		2	..	..		2	..	..
	3	..	..		3	106	55		3	..	..		3	..	..		3	..	..
	4	216	48		4	287	455		4	151	330		4	73	17		4	..	..
	5	202	66		5	341	630		5	149	305		5	94	14		5	25	28
	6	126	83		6	578	520		6	163	280		6	..	..		6	266	97
3	1	390	95	3	1	48	65	3	1	536	90					3	1	94	29
	2	..	..		2	..	..		2	..	..						2	..	..
	3	692	..		3	..	..		3	..	..						3	..	..
	4	1103	..		4	211	55		4	12	545						4	271	81
	5	1145	150		5	83	50		5	..	450						5	123	63
	6	491	95		6	16	21		6	..	475						6	..	..

* Oil instillation was done after the second sample in each case.
† P, phosphatase; B, bile concentration.

the other hand, in some patients with pancreatic insufficiency the phosphatase activity and bile concentration are in inverse proportion. In five patients with biliary atresia an extremely wide range of alkaline phosphatase values was obtained.

Serial duodenal fluid samples were obtained from 28 patients after the intraduodenal instillation of olive oil. This procedure was primarily designed to test the response of the pancreatic digestive enzymes to this stimulus which at the same time stimulated the flow of bile from the gall bladder. At least two, and as many as six, separate samples collected at 20-minute periods were obtained from each patient. In general, the digestive enzymes showed an increase in activity in all patients except those with complete or partial pancreatic insufficiency. Table 3 shows the relationship of the bile concentration to the alkaline phosphatase activity in 14 selected patients. There is a great variation and dissociation in the bile and phosphatase values obtained in any one person in successive samples, regardless of the underlying condition. In some patients a marked increase in phosphatase is noted, although there is practically no increase in bile concentration. In patients with mucoviscidosis in whom there is no digestive enzyme response, one notes an increase in the alkaline phosphatase as well as an increase in bile concentration. The two patients with celiac disease merit comment for the relatively low values shown for both phosphatase and bile. In line with other observations, the volume of fluid obtained per unit time in these patients is greater than average.

An attempt was made to study the effect of trypsin on alkaline phosphatase as found in duodenal fluid. In four fluids with high phosphatase activity the addition of crystalline trypsin did not influence the phosphatase activity. This is in agreement with the findings of Schmidt and Tannhauser.[7]

The results of the acid phosphatase determinations show the same dissociation in relation to the concentration of bile and to the activity of the digestive enzymes and to the activity of the alkaline phosphatase. The variation in activity was great and could not be correlated with the nature of the illness or the age of the patient.

COMMENT

The alkaline phosphatase as found in duodenal fluid may be derived from three main sources: (1) It may come from the duodenal mucosa itself; (2) it may be secreted by the liver, or (3) it may come from the pancreas. The intestinal mucosa is extremely rich in alkaline phosphatase and may actually represent one of the areas of highest concentration in the body.[8] The concentration also appears to be high in the duodenum, where the greatest digestive activity takes place. The alkaline phosphatase may reach the intestinal lumen as a result of desquamation of epithelium cells or by the process of secretion. Studies by Manheimer and Seligman[9] and Landing,† who used histochemical staining techniques, have shown high concentration of enzyme in the duodenal mucosa. Unpublished observations of Landing show that in patients dying with mucoviscidosis abundant alkaline phosphatase is present in the duodenal mucosa. He also finds phosphatase-staining material in the lumen of the intestine. These observations support our findings. It is believed that the "phosphatases" in the intestinal mucosa are concerned with the absorption of hexoses, fatty acids, and amino acids.[10]

Alkaline phosphatase is produced in the centroacinar cells of the pancreas and is secreted with the digestive enzymes. It is found in pure pancreatic juice from humans in a quantity of 2.1 to 3.8 units/100 ml.[11] as well as in some animals (0.4 to 12.0 units/100 ml.)[12] and is secreted in an active form. The concentration of alkaline phosphatase in pancreatic juice is not influenced by the serum alkaline phosphatase level.[12]

In view of the multiple sources of alkaline phosphatase in the duodenal fluid and the much greater activity of duodenal secretion as compared to the activity of either bile [13] or pancreatic juice, the duodenal phosphatase activity may not serve as a reliable index of pancreatic function. The possible role of in-

† Landing, B.: Personal communication to the authors.

hibitor or accelerator substances normally found in duodenal fluid may complicate the interpretation still more.[14] In addition, numerous factors influence the phosphatase activity of tissues and fluids. Determining factors may be related to age, rate of growth, central nervous system disease, endocrine function, bone disease, vitamin deficiency, and diet. Some of these influences may play a role impossible to evaluate in the material presented.

SUMMARY

The alkaline phosphatase activity of duodenal fluid is independent of the bile concentration and independent of the activity of the digestive pancreatic enzymes. A wide range of activity of alkaline phosphatase was found in patients with complete absence of digestive enzymes. In those instances of partial pancreatic insufficiency a similar wide range of activity was encountered. Contrariwise, there were some instances in which there was high activity of the digestive enzymes with no activity of alkaline phosphatase.

It was felt that a good deal of the alkaline phosphatase normally encountered in the duodenal fluid arises from the duodenal mucosa itself. This evidence is indirect and is gathered from the cases of biliary atresia and pancreatic achylia in which there is high phosphatase activity of the duodenal fluid. It is further supported by the evidence that the concentration of bile or of the digestive enzymes is independent of the concentration of phosphatase.

The increase of alkaline phosphatase activity of the duodenal fluid in patients with pancreatic insufficiency following oil stimulation, in which there is no increase in bile, indicates that the oil may have a stimulating or irritating effect on the duodenal mucosa.

There appears to be no correlation between the activity of acid phosphatase and the activity of the digestive pancreatic enzymes, alkaline phosphatase, or bile concentration.

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Piperazine in the Treatment of Enterobiasis

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Enterobiasis is the most common helminth infestation in the United States. The pinworm has proved to be a difficult parasite to eradicate for the human race. Although reports of therapeutic agents have filled the medical literature throughout the years, not one drug has been universally accepted. Cram [1] gave the following criteria for a satisfactory agent:

1. The drug must be highly effective in removing pinworms.

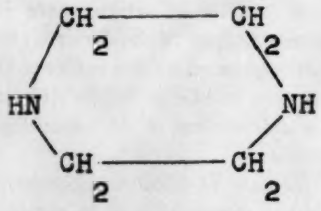
2. The drug must be relatively nontoxic, so that it can be given in repeated treatments over a period during which viable pinworm ova may be present in the patient's surroundings, the repeated administration of the drug also assuring its entrance into the cecum and appendix, common sites of pinworm infection.

3. The treatment must be of such reasonable cost that its use in large families will not be prohibitive.

4. The treatment must be so easily administered that it can be used with a minimum of effort in large household groups.

There are numerous objections to many of the medications now used in the treatment of enterobiasis. Methylrosaniline chloride (gentian violet), although curing up to 90%, has a high incidence of side-effects, notably gastrointestinal disturbances, and the enteric-coated tablets through which the drug is administered may be difficult for small children to swallow. Oxytetracycline (Terramycin) is of value in a large number of patients but is expensive and may cause side-reactions and sensitization to the antibiotic. Hexylresorcinol has not been efficacious. Phenothiazine, although effective in enterobiasis, causes a large number of toxic reactions. Diphenan (parabenzylphenylcarbamate) and Egressin (thymyl-*n*-isoamylcarbamate) are not efficient agents for the treatment of pinworms.

Recently piperazine has entered the armamentarium of therapeutic agents available for the treatment of enterobiasis. It was first introduced into medicine for the treatment of uric acid calculi and gout because of its ability to dissolve uric acid in the test tube, but was not proved successful. Piperazine is a colorless hygroscopic material which forms crystals that are freely soluble in water and glycerin. It is diethylenediamine and has the following structure:



It is strongly alkaline and combines with acids to form salts. All oxidizing agents decompose it, and it is incompatible with alkaloids.[2]

Piperazine was used on mice in the treatment of Aspicularis tetraptera and Syphacia obvelata, which are related to the pinworm, by Mouriquand and his co-workers,[3] Standen,[4] and Brown and his co-workers.[5]

Mouriquand and his co-workers [6] treated a group of children having pinworms with piperazine hexahydrate and obtained a satisfactory number of cures. Rouques [7] used a

The piperazine used in this study was supplied by Burroughs Wellcome & Company as Syrup of Antepar.

From the Department of Pediatrics, 1600th U.S.A.F. Hospital, Westover Air Force Base, Mass.

Present address: Children's Medical Center, 300 Longwood Ave., Boston 15 (Dr. Rachelson).

similar treatment routine and found it to be effective against gravid female pinworms. White and Standen [8] treated 108 children with enterobiasis with piperazine hydrate and found a daily dosage of 100 mg. per year of life gave a 54% cure rate, and a higher daily dosage of 250 mg. per year of age cured 84%. Dosages as high as 150 mg/kg/day were well tolerated. They calculated a weight/dose cure rate of 97%, using a daily dosage which exceeded 50 mg/kg. Bumbalo and his co-workers [9] administered piperazine hexahydrate to 47 children who had enterobiasis and cured 85% of their patients with no evidence of toxicity. Basnuevo [10] found piperazine to be effective in curing over 90% of his patients with pinworms with relatively little toxicity.

Enterobiasis has been a major problem among dependent children in the military service. We recently found an incidence of 31.5% infestation with Enterobius vermicularis among children up to 12 years of age at the pediatric section of the 1600th U. S. A. F. Hospital, Westover Air Force Base, Mass.[11] Because of recent evidence reporting the success of piperazine with relatively few side-effects, we decided to evaluate this drug in our cases.

METHODS AND MATERIALS

One hundred and fifty patients infected with E. vermicularis were treated with piperazine citrate at the outpatient clinic of the 1600th U.S.A.F. Hospital, Westover Air Force Base, Mass. There were 53 males and 82 females in the series. Of this number, 138 were children ranging in age from 10 months to 13 years. The remainder were young adults, none older than 39 years. Two of the adults treated were pregnant, one in the second trimester and the other in the third. In all instances the diagnosis was confirmed by a Scotch Cellophane tape swab of the perianal area as devised by Graham,[12] and pinworm ova were seen in all cases which we treated. In a household infested with enterobiasis, we did not treat all members of the family, but only those who demonstrated pinworm ova on any of three consecutive daily perianal swabs which were made.

The medication used for treatment was piperazine citrate. We used an orange-flavored syrup containing piperazine citrate in an amount equivalent to 100 mg. piperazine hexahydrate per cubic centimeter, or 500 mg. per teaspoon. The medication was given for seven consecutive days, followed by a rest period of one week, with a second course of treatment of seven days' duration immediately following the rest period. The dosages used were given according to the following schedule:

Children up to 15 lb. (6.8 kg.) body weight, 250 mg. once daily

Children 15-30 lb. (6.8-13.6 kg.) body weight, 250 mg. twice daily

Children 30-60 lb. (13.6-27.2 kg.) body weight, 500 mg. twice daily

Children over 60 lb. body weight and adults, 1000 mg. twice daily.

In addition to the medication, all patients were given the following instructions for strict personal care and sanitation:

1. Scrub the hands and fingernails well with soap and a brush before each meal and after toilet.
2. Keep the fingernails short and well scrubbed.
3. Keep the fingers away from the mouth and nose.
4. Sterilize all metal toys and similar objects in a hot oven, and keep all toys out of the mouth.
5. Scrub toilet seat after use.
6. Shower each morning, washing the rectal area, genitalia, and areas around them well.
7. Wear snug cotton underpants under bedclothes at night.
8. Use separate towel and wash cloth for face.
9. Change soiled bed linen, underwear, bedclothes, towels, and washcloths daily. Either boil all linen well or soak in a household ammonia solution (2 teacups to 10 gal. water) for one hour.
10. Air all rooms for two hours daily.
11. Vacuum rooms daily.

At the end of the third week, after the second course of piperazine, three daily consecutive perianal Cellophane tape smears were taken upon awakening and examined for pinworm ova. If no ova were seen on any of the three smears, the patient was considered cured. On the other hand, a treatment failure was based on the presence of pinworm ova.

RESULTS

Of the 150 patients treated in our series, only 16 demonstrated pinworm ova on the perianal smears taken at the end of the third week after the second course of treatment with piperazine. The result was an initial

TABLE 1.—*Results of Treatment with Piperazine*

	No. of Cases	No. of Cures	Course of Treatment	Cure Rate
	150	134	7 days treatment 7 days rest 7 days treatment	89.3% (Initial cure rate)
	12 *	12	7 days treatment 7 days rest 7 days treatment 7 days additional treatment	100.0%
Total	150	146		97.3% (Over-all cure rate)

* Cases which failed on original course of therapy and received seven additional days of piperazine therapy.

cure rate of 89.3% (Table 1). We treated 12 of the 16 patients who were found to be still infested with enterobiasis with an additional week of medication immediately following the second course of treatment, using the same dosage and hygienic precautions as before. At the end of this additional week of treatment, perianal smears were similarly taken daily for three days. All of the 12 patients receiving the extra treatment were cured at the end of the week, and none had any ill effects. Thus the over-all cure rate was 97.3%, bringing the total number of cures to 146. The sex and age of the patient had no bearing on the cure rate.

In each patient the dosage of piperazine given in milligrams per kilogram of body weight was calculated to determine any effect on the cure rate (Table 2). The majority of our series was treated with piperazine in dosages from 26-55 mg/kg. of body weight. The lowest dosage given was 15 mg/kg. of body weight, and the maximum was 71 mg/kg. The amounts of piperazine administered in this series made no appreciable difference on the cure rate, and similar results were obtained with large variations of the dosage. All of the side-effects which resulted occurred in patients receiving 26-50 mg/kg. of piperazine, and in no instance was a side-effect noted using a dosage greater than 50 mg/kg.

TABLE 2.—*Effect of Piperazine Dosage on Cure Rate*

Dose (Mg/Kg. Body Wt.)	No. of Patients	Initial Cure Rate, Per Cent	Over-All Cure Rate, Per Cent	Side-Effects
15-20	1	100.0	100.0	None
21-25	4	100.0	100.0	None
26-30	15	93.3	93.3	Diarrhea, 1 case
31-35	18	94.4	100.0	Urticaria, 1 case; nausea, 1 case
36-40	34	94.1	100.0	None
41-45	27	81.8	92.6	Urticaria, 1 case; erythema multiforme, 1 case
46-50	25	96.0	100.0	Urticaria, 2 cases
51-55	13	84.6	100.0	None
56-60	4	50.0	100.0	None
61-65	5	80.0	80.0	None
66-70	3	66.6	100.0	None
71-75	1	100.0	100.0	None
Total	150	89.3	97.3	

Side-effects were evidenced in only seven patients. There were four instances of urticaria, three of the cases occurring shortly after the completion of the second course of treatment and one of a day's duration, occurring on the second day of the first course of treatment. One mild case of erythema multiforme occurred three days after completion of therapy and cleared within a few days. One patient experienced a mild diarrhea during the piperazine treatment which responded rapidly to therapy, and one patient had slight nausea and lethargy while taking the drug. Three of the four patients evidencing urticaria were given a placebo of the orange-flavored vehicle to determine whether the urticaria was due to the vehicle, but none had any further urticaria. The urticaria may be attributed to either the absorption of foreign proteins derived from the dead worms or to an allergy to the piperazine. None of the 12 patients who received additional therapy had any side-effects. The dosage of piperazine given to the patients was unrelated to the incidence of side-effects observed. Complete blood cell counts and urine examinations were performed on 25 of our patients, including those with urticaria and erythema multiforme. No abnormality of the blood or urine was found in any case. The drug was taken readily by the bulk of our patients and was palatable. There were no ill effects in the two pregnant women treated, one of whom delivered a normal infant one week after completion of therapy.

COMMENT

Piperazine, in our experience, has proved to be a satisfactory agent for the treatment of enterobiasis. The drug fulfills the criteria of Cram for a therapeutic medication, as mentioned previously. An over-all cure rate of 97.3% was obtained, which is superior to that usually obtained after treatment with other drugs used in the therapy of this disease. We have found that an additional week of medication, in treatment failures, after the normally prescribed course, was effective in eradicating the pinworm in all 12 patients who were so treated.

Piperazine is relatively nontoxic and can be given safely without any need for routine laboratory testing. The toxicity rate of patients treated was 4.6%. Urticaria, the most frequent side-effect, usually occurred after the completion of treatment and most often cleared in one or two days after antihistamines were administered. Gastrointestinal complaints, which are prominent with some of the other therapeutic agents used, are notably absent after piperazine therapy.

Satisfactory cures may be obtained with drug dosages in the range of 25-50 mg/kg. of body weight. Although others have recommended higher dosages of the drug, none have had cure rates as high as ours. Because of the smaller amount of medication which we feel is required, the treatment is of reasonable cost. It was found to be of special value in the treatment of infants and small children who previously could not be given medication in a palatable liquid which would be taken readily. An additional advantage is that piperazine is given at meal times and not one hour before as is the usual practice with methylrosaniline chloride (gentian violet).

SUMMARY

One hundred fifty patients with enterobiasis were treated with piperazine. A cure rate of 97.3% was obtained. Side-effects occurred infrequently, and those that did appear were mild. We find piperazine to be more efficacious in the treatment of enterobiasis than any other medication previously reported.

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Case Reports

IMPERFORATE ANUS IN BROTHERS

J. LAWRENCE COCHRAN, B.Sc., M.D., Carroll, Iowa

ON JULY 5, 1951, at the local hospital, I delivered spontaneously after a mesiolateral episiotomy on a 22-year-old primipara a living male child whose birth weight was 6 lb. 2 oz. (2780 gm.) Routine inspection of this newborn infant disclosed an imperforate anus. All oral fluids were immediately interdicted. A short time later, x-ray of this baby in the head-down position in accordance with the Wangensteen-Rice method [1] showed a gas bubble at the blind end of the intestinal tube within 1½ in. (3.8 cm.) of the normal location of the anal orifice. This baby was taken posthaste to a large Midwestern clinic, where definitive surgical repair of his proctological defection was accomplished before the baby had attained an age of 24 hours. At the present time, this child appears and acts as an entirely normal 3-year-old boy and enjoys normal physiologic functions of the anorectal organs.

On Sept. 6, 1954, at the same hospital, I delivered this same mother of her second child, another boy, whose birth weight was 7 lb. 8 oz. (3400 gm.). (The father of these two children is also the same man.) A few moments after the birth of this second child, the routine newborn inspection disclosed another imperforate anus, which subsequent x-ray examination proved to be also of Type 3 by the Ladd and Gross classification.[1] The only difference (other than the matter of initial birth weights) in these two children was that the distance between the blind end of the intestinal tract and the normal site for the anal orifice was only 1 in. (2.5 cm.) in the second child. This second child was taken to the same surgeon at the same Midwestern clinic, where almost identical reparative procedures were accomplished before the second baby had yet attained an age of 24 hours.

No other child was born to this couple in the interim between the dates of the two parturitions cited above.

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BRONCHIAL OBSTRUCTION DUE TO MISPLACED LEFT PULMONARY ARTERY

HARRY R. MORSE, M.D., Knoxville, Tenn.
and
SAM GLADDING, M.D., Philadelphia

WITH THE increasing awareness of cardiovascular anomalies and the widening scope of surgical procedures to correct these abnormalities, it is imperative to report rare cases. The proper management of such cases demands a sharing of the experiences of others. This case report is the second in the literature.[1]

Baby Glen V. N., a term pregnancy and uneventful delivery, secondborn white boy, was noted to have dyspnea and wheezing from birth, with cyanosis unless given continuous oxygen.

Initial examination revealed decreased to absent breath sounds over the entire right lung field and inspiratory retraction with audible wheezing. The heart did not seem to be displaced. When the infant was five hours old, attempts at aspiration were productive of only a very small amount of mucous, and clinically the infant was deemed worse following the procedure. The subsequent course showed partial return of breath sounds over the right lung field, with some decrease in the wheezing. X-rays were taken and interpreted as an atelectasis of the right lower lobe and the left upper lobe. The weight of the infant at this time was 7 lb. 11 oz. (3490 gm.), his birth weight not having been taken because of his critical condition. Reexamination when the infant was 10 days old revealed in addition to the previously mentioned findings marked hyperresonance over the right lung field and a shift of the heart and mediastinum to the left; respirations were rapid and shallow, and inspiratory retraction was clearly seen both above and below the costal cage. With the initial clinical impression of a partial obstruction of the right main-stem bronchus, a left upper-lobe atelectasis, and possible congenital heart disease, the infant was transferred to Temple Unversity Hospital for further study and treatment.

The initial chest x-ray at this hospital revealed an obstructive emphysema of the right lung, causing marked herniation of the mediastinum into the left thorax.

Bronchoscopy revealed that the lumen of the right bronchus was very narrow, and only a few bubbles of air passed on expiration. It was the bronchoscopist's opinion that there was kinking of the right main bronchus.

The baby's subsequent course during the next several weeks was stormy, with many spells of cyanosis and dyspnea, and it was felt in spite of the infant's poor condition that surgery was the only hope of salvation.

OPERATION

Under endotracheal anesthesia, the right chest was opened, and it was found that the right lung expanded and deflated freely. On exploration, an anomalous vessel was found crossing the right main bronchus just distal to the carina, and it was decided that this represented a left pulmonary artery encircling the right main bronchus. There appeared to be three courses open. The first would be a right pneumonectomy; second, ligation of the vessel; third, transplantation of the artery to relieve the pressure. The latter was decided upon, and an attempt was made to free the artery and attach it to the lower trachea. This was accomplished, and the compression appeared to be lessened.

Immediately after the operation the infant showed improved aeration of the right chest, and there was a notable decrease in the respiratory effort. This condition was only transient, however, and the infant soon experienced recurring episodes of dyspnea and cyanosis, necessitating intratracheal oxygen and artificial respiration. Death occurred during one of these periods of dyspnea, 11 days after operation.

Autopsy findings * revealed no evidence of pneumothorax on either side. The left pleural cavity was free of adhesions and fluid and was approximately one-half filled by the left lung.

The right pleural cavity contained approximately 7 cc. of blood. The right lung was hyperexpanded and extended across the anterior aspect of the pericardium to a point just to the left of the left internal mammary artery.

From the Departments of Bronchoesophagology and Pediatrics, Temple University Hospital, Philadelphia.

* Postmortem examination was done by Dr. James B. Arey, St. Christopher's Hospital for Children, Philadelphia.

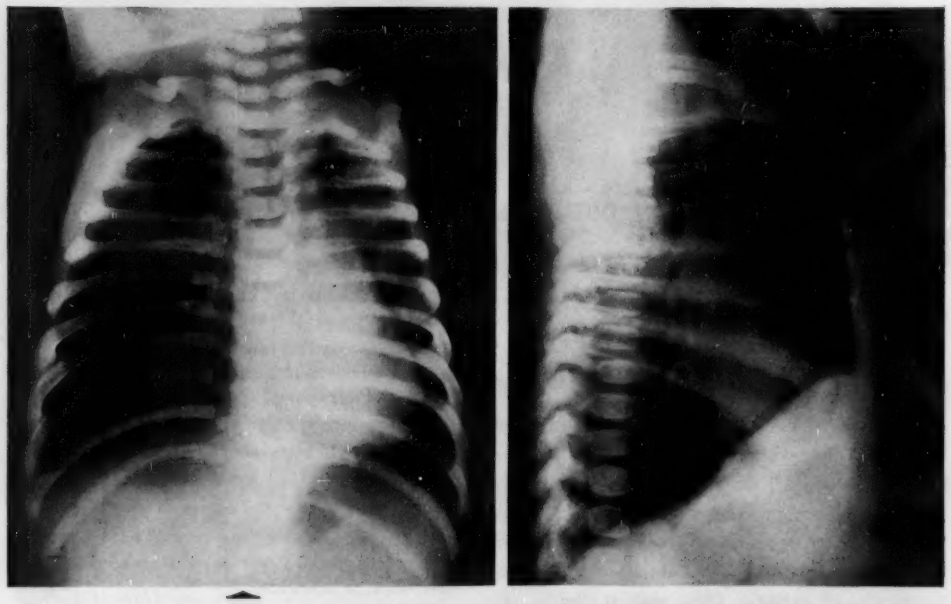
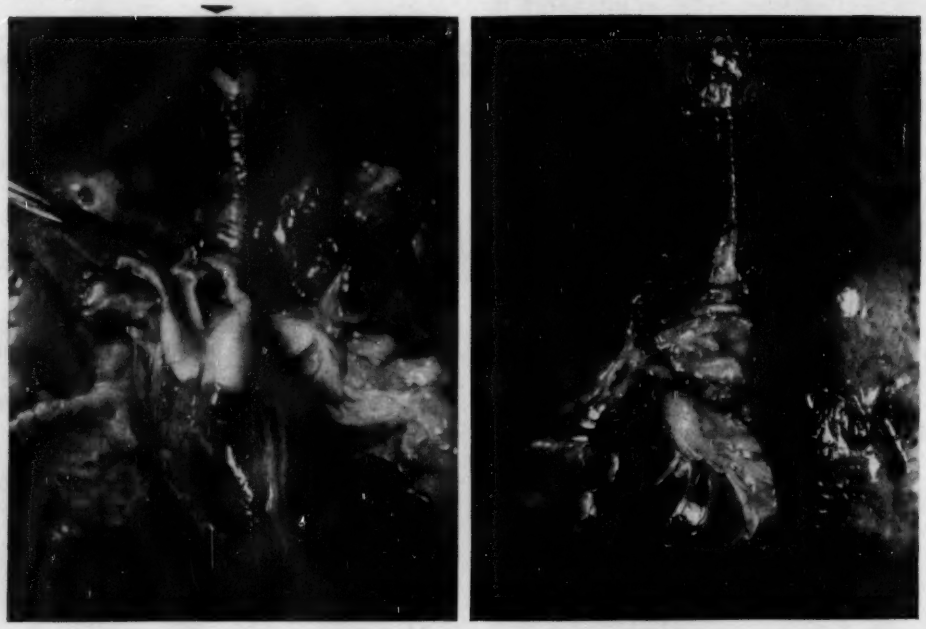


Fig. 1.—Left, roentgenogram of the chest, showing obstructive emphysema on the right, with shift of the mediastinum and heart to the left side. A small area of pneumonitis is present in the right upper lung field. Right, lateral view of the chest, showing the mediastinal herniation anterior to the heart shadow.

Fig. 2.—The opened chest, showing the marked obstructive emphysema of the right lung.

Fig. 3.—Left, postmortem view of the heart and lungs from the anterior aspect, showing the left pulmonary artery coursing anterior to the trachea to wrap around the right main bronchus. Right, posterior view of the heart and lungs, showing the left pulmonary artery going around the right main bronchus and then posterior to the trachea to supply the left lung.



The pulmonary artery, aorta, and great vessels of the aorta arose from their usual sites. The ductus arteriosus was in normal position. However, at the level of the pulmonary end of the ligamentum arteriosum no left pulmonary artery arose from the main pulmonary artery. Instead, the common pulmonary artery swung to the right and slightly posteriorly for a distance of approximately 0.5 cm., where it branched into a right and a left pulmonary artery. The right pulmonary artery was normal in position.

The left pulmonary artery originated just anterior to the right main bronchus, coursed over the superior aspect of this structure at the origin of the bronchus from the trachea, then passed to the left lung behind the left main bronchus. At the point where this vessel crossed the bronchus the artery was found to measure 0.5 cm. in diameter and to be sutured to the posterior lateral wall of the trachea 1 cm. above the bifurcation. At the point of crossing by the anomolous left pulmonary artery, the right main bronchus exhibited a narrow zone of constriction in its superior wall. The artery apparently compressed the bronchus from above and posteriorly.

At the point of compression the bronchus measured 0.7 cm. in external diameter, and distal to this, 0.9 cm. in external diameter. Although there was a suggestion of softening of the bronchial wall at the region of the constriction, it was not definite, and firm cartilage rings were still present in the bronchial wall at that level.

The ductus anteriosus was found closed at both the pulmonary and the aortic ends. The foramen ovale was closed, and no interventricular septal defects were noted.

There was no evidence of intracranial disease.

710 Hill Ave., S. W.

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News and Comment

ANNOUNCEMENTS

Three-Day Course at Memorial Center for Cancer and Allied Diseases.—Memorial Center for Cancer and Allied Diseases, Pediatrics Department, announces a comprehensive three-day course, on April 27, 28, and 29, 1955, for pediatricians, general practitioners, and health officers. Current developments and established methods in diagnosis, differential diagnosis, and management of benign and malignant tumors, Hodgkin's disease, leukemia, and reticuloendotheliosis in childhood are included. The course will include ward rounds, seminars, demonstrations, and examinations of children in pediatric, surgical, chemotherapy, and radiotherapy clinics. The faculty will consist of 20 members of the Attending Staffs of Memorial Hospital and Sloan-Kettering Institute for Cancer Research. The class will be limited to 15 physicians.

For information, address Director, Pediatric Service, Memorial Center, 444 E. 68th St., New York.

PERSONAL

Election of Dr. Robert E. Burns.—Dr. Robert E. Burns, chairman of the section on orthopedic surgery at the University of Wisconsin Medical School, has been elected president of the International Society of Orthopedic Surgeons and Traumatologists, it was announced today by society headquarters, Brussels, Belgium. Dr. Burns' term is for the year 1955-1956.

Changes in University of Wisconsin Medical School Faculty.—The University of Wisconsin regents Saturday approved an interim appointment of Dr. Otto A. Mortensen to the post of acting dean of the University of Wisconsin Medical School from March 1 to June 30. He is now associate dean of the school.

In a parallel action, the regents granted Dean William S. Middleton a one-year leave of absence, effective March 1, to permit him to become chief medical director of the U. S. Veterans Administration at that time.

Before his call to the federal agency, Dean Middleton had resigned his Medical School deanship, effective July 1, to devote his energies to research and teaching. Dr. John Z. Bowers, now dean of the University of Utah School of Medicine, is scheduled to take over the Wisconsin Medical School deanship July 1.

DISSEMINATED JUVENILE FIBROUS DYSPLASIA OF THE JAWS

RALPH E. McDONALD, D.D.S., M.S.
and
WILLIAM G. SHAFER, D.D.S., M.S., Indianapolis

CERTAIN bone dysplasias of the mandible and maxilla frequently present a unique challenge in diagnosis and treatment because of their pathogenetic dissimilarity yet microscopic similarity to lesions in other bones. Numerous such lesions of the jaws have been described in the literature under a variety of terms, although the present trend is toward classifying many of these under one category: fibrous dysplasia.

While the central giant-cell tumor of the jaw still probably represents a distinct entity, it has been pointed out by Waldron [1] and many others that, in the light of present knowledge, some lesions previously diagnosed as such would today be called fibrous dysplasia. To eliminate the connotation of the term "tumor" and to describe better the true nature of the lesion, Jaffe [2] has suggested the term "giant cell reparative granuloma" for certain of these conditions. It is not the purpose here to attempt to review the literature on fibrous dysplasia and giant-cell lesions of the jaws, but rather to present a rare variant, very few of which have been previously described.

In 1933, Jones * reported a case of "familial multilocular cystic disease of the jaws" in three children of the same family. He coined the term "cherubism" to describe their unusual clinical appearance and facial deformity. Jones,[6] in 1938, reported a similar case in a young child, in which the condition was traced through five generations. Waldron [7] has also reported three cases in one family under the term "bilateral giant-cell tumor." His cases, from the clinical, roentgenographic, and histologic point of view, were very similar, if not identical, to those reported by Jones. Talley [8] has reported a case of fibrous dysplasia of the jaws in a mother and her 3½-year-old child. He pointed out that any treatment was contraindicated until early adult life, at which time the disease apparently becomes static or regresses. Five cases occurring in members of two families have been reported by Caffey and Williams.[9] The disorder was characterized by massive swelling of the cheeks and jaws and defective dentition, but without any associated symptoms or systemic manifestations. A recent case reported by Brannin and Christensen,[10] and termed "bilateral giant cell tumor," occurred in siblings and might be related to the condition which was originally described by Jones.

The case to be reported here, after careful evaluation of the physical, roentgenographic, and histologic findings, appears to be identical to those of Jones, and possibly those of Waldron and Brannin, even though the familial pattern is absent.

REPORT OF A CASE

History.—A 5-year-old white girl was presented at the University Dental Clinic with the chief complaint of "swelling of the jaws, progressive loss of teeth over a three-year period and difficulty with speech." The parents stated that the child's jaws had always been large. There was no evidence of a similar oral condition or facial deformity in their three younger children or in any relative on either side of the family. There was a past medical history of only the usual childhood diseases.

Physical and Oral Findings.—The child appeared as a fairly well-nourished averagely developed white girl with obvious symmetrical enlargement of the cheeks (Fig. 1). Hard masses due to bilateral bulging of the bone of the mandible could be felt on palpation.

From the Departments of Pedodontics and Oral Pathology, Indiana University School of Dentistry.

* References 3-5.

Fig. 1.—Enlargement of the cheeks due to bilateral bulging of the bone of the mandible.

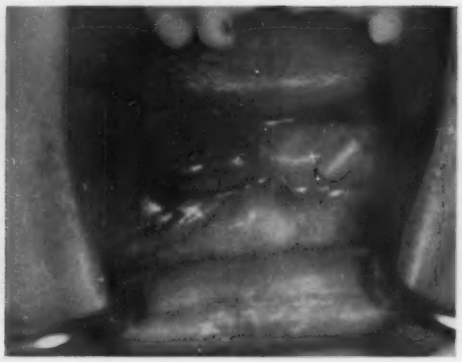
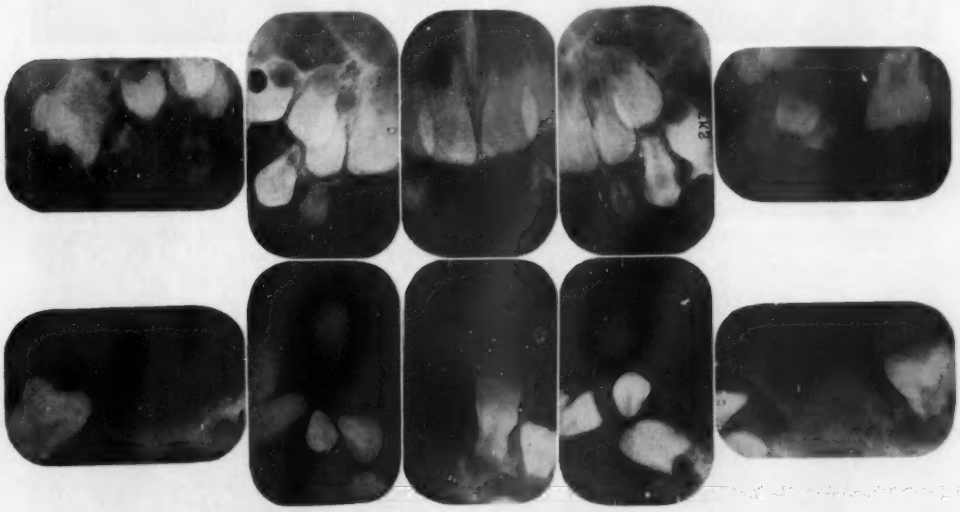


Fig. 2.—An ulcerated hemorrhagic-appearing mass in the area of the lower right incisor area. A permanent incisor on the left side has been displaced by the bulging mass.

Oral examination revealed a mandibular incisor and six maxillary deciduous teeth. There was an ulcerated hemorrhagic-appearing mass in the area of the lower right lateral incisor (Fig. 2). This mass was not painful, there being no specific complaint on the part of the child. All of the mandibular deciduous teeth were missing as a result of spontaneous loosening and having been "picked out by the child." The mandibular and maxillary alveolar ridges were felt as hard bulging painless masses.

Roentgenographic Findings.—Full mouth radiographs demonstrated a large area of bone destruction in the anterior portion of the mandible and displacement of the developing permanent teeth (Fig. 3). A number of permanent teeth were missing—the mandibular bicuspids and second molars and the maxillary second bicuspids and second molars. There appeared to be normal morphological development of the unerupted teeth. Lateral jaw (Fig. 4) and head-plate roentgenograms (Fig. 5) demonstrated multilocular cystic involvement of the man-

Fig. 3.—A full mouth roentgenogram demonstrating large areas of bone destruction and several missing teeth.



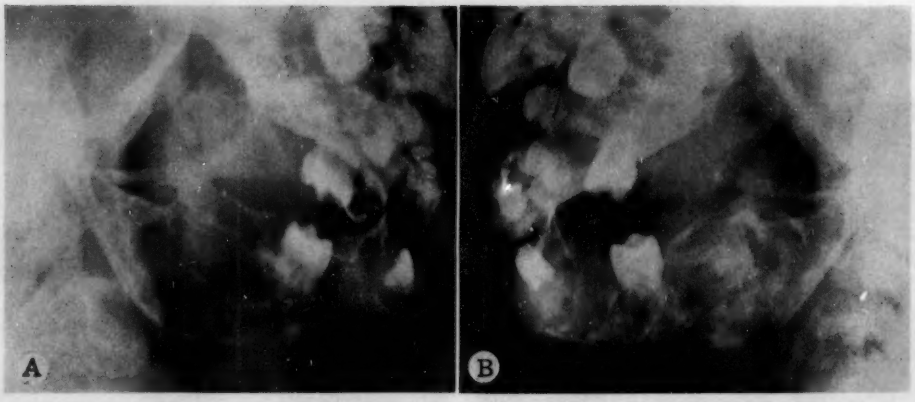


Fig. 4.—Lateral jaw roentgenograms demonstrating multilocular cystic involvement of the mandible and maxilla.

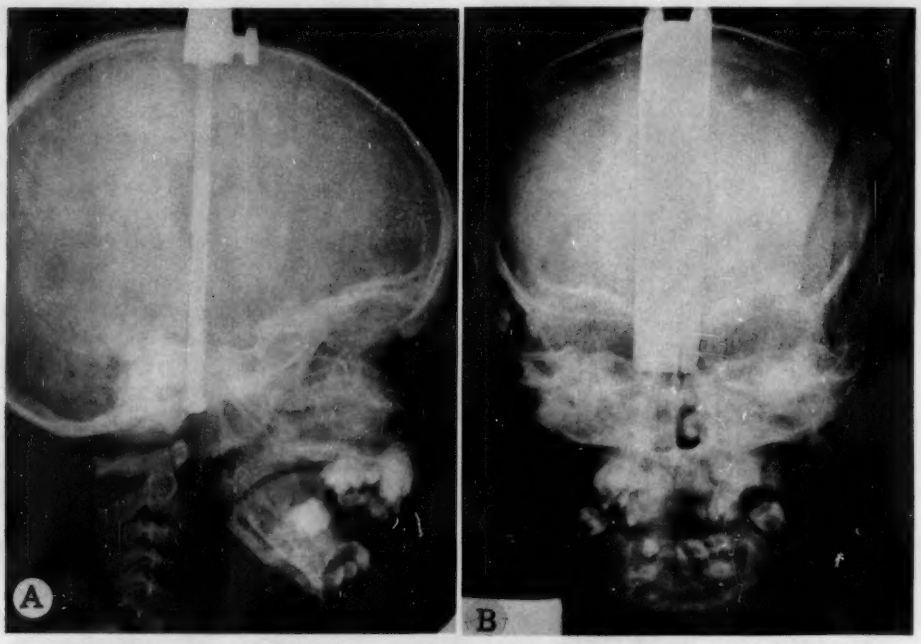
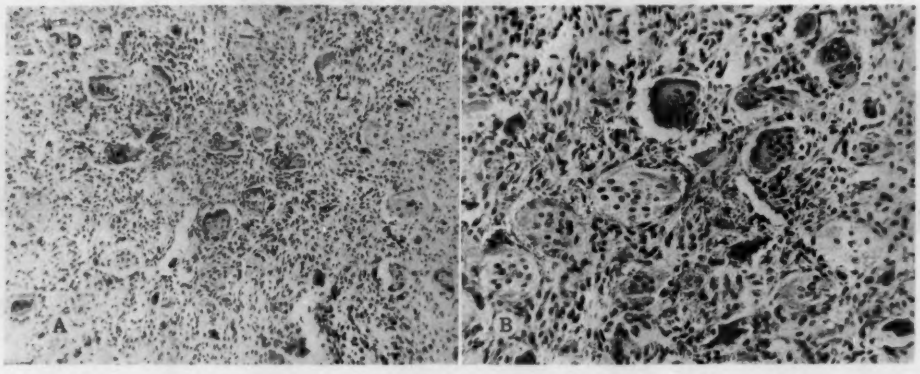


Fig. 5.—Lateral and anteroposterior cephalometric roentgenograms. *A*, displacement of the mandibular anterior teeth in a large area of bone destruction. Multilocular cystic involvement of the mandible and maxilla and many missing teeth. *B*, abnormal bulging of the mandible.

Fig. 6.—Histologic soft-tissue section. *A*, the cellular nature of the lesion is illustrated, as well as the large number of multinucleated giant cells scattered diffusely throughout the specimen. *B*, the vascularity of the tissue and the general lack of osteoid structure may be noted under higher magnification.



dible and both maxillae. A complete skeletal survey failed to reveal similar lesions in any other bones.

Microscopic Findings.—A biopsy was made of the soft-tissue lesion in the anterior region of the mandible. A second section was taken from within the body of the mandible and included a segment of soft tissue as well as a small segment of bone. The soft-tissue section demonstrated a large number of multinucleated giant cells scattered diffusely throughout a very cellular stroma (Fig. 6*A*). The giant cells were large and irregular in shape and contained up to 30 or 40 nuclei (Fig. 6*B*). There were many thin-walled blood vessels scattered throughout the specimen, and a mild sprinkling of polymorphonuclear leucocytes was seen throughout the connective tissue. The changes noted were those of fibrous dysplasia, compatible with those seen in familial multilocular cystic disease of the jaws. The second section appeared histologically identical to the first biopsy.

Laboratory Findings.—The blood chemistry picture was essentially normal, with serum calcium being 10.7 mg. per 100 cc. and phosphorus, 6.0 mg. per 100 cc. This seemed to rule out the possibility of the bone dystrophy being related to hyperparathyroidism. The complete blood cell count and urinanalysis, including mercury content, were also within normal limits.

COMMENT

A case has been observed which from the clinical, roentgenographic, and histologic study appeared similar to giant-cell tumors of the jaw bones. It is felt, however, that true giant-cell tumors of the jaws are very rare. Lichtenstein [11] has stated that the odds are overwhelmingly against the diagnosis of a giant-cell tumor in a child or adolescent. Coley [12] has also reported that giant-cell tumors are seldom encountered in patients under 20 years of age, and he believes that lesions resembling giant-cell tumors in the child are either cysts or areas of fibrous dysplasia.

This case reported resembles in every way that which was first reported by Jones, in 1933, and for which he coined the term "cherubism" but diagnosed as "familial fibrous dysplasia of the jaws." However, there is no evidence to indicate that the case reported here follows a familial pattern, as did Jones's original cases.

One outstanding similarity in all cases is the absence of a number of permanent teeth. Rather than this being a coincidental observation, it is probable that the dystrophy is related to odontogeny and thus is not unlike a hamartoma, which has been defined as a tumor-like mass resulting from faulty embryonal development of cells and tissues natural to the part.

It is improbable that the destructive process could have been responsible for the absence of so many teeth yet leave intact several morphologically normal permanent teeth. While it is likely that the destructive process was responsible for the loosening and spontaneous loss of many of the deciduous teeth, there is nothing in the history to account for the apparent absence of so many permanent tooth buds.

Since little is known concerning the etiology of cases of fibrous dysplasia of the jaws, the treatment must be empirical. While the treatment of choice for true giant-cell tumors is curettage followed by cauterization, that type of treatment is not practical in this case, due to the extensive involvement of both the mandible and maxilla.

During a 10-month observation period there has been no progression of the bony lesions; in fact there is some evidence of regression of the lesions in the mandible. In view of this it is believed that surgical treatment should be undertaken only at a later date and for the purpose of improving the cosmetic appearance.

SUMMARY AND CONCLUSIONS

A case of fibrous dysplasia of the jaws is reported, and its similarity to several other cases is discussed.

It is possible that the condition may follow a familial or genetic pattern.

While the etiology is unknown, there is evidence that the condition is related to odontogeny.

Fibrous dysplasia of the jaws, which may be congenital, apparently progresses rapidly during early childhood but later may remain static or even show evidence of slight regression.

Surgical reduction of the bulging masses in the jaws may be undertaken for correction of the grotesque deformity.

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ADVENTITIOUS DEPOSITION OF IODIZED OIL IN MIDDLE EAR

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and
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IODIZED oil (Lipiodol) has been used by us as an opaque medium for the visualization of the esophagus and the gastrointestinal tract in newborns and infants. It has been observed by others as well as ourselves that the medium is frequently aspirated into the trachea and bronchial tree.* We have been observing a patient for one and one-half years in whom radiopaque particles were found in the right middle ear and mastoid region following a gastrointestinal series which was done with iodized oil. We have found no other similar case in the literature.

REPORT OF A CASE

L. S. (220907), a girl, was born in Bronx Hospital Oct. 4, 1952, after a difficult delivery. Soon after birth the child exhibited muscular rigidity and was noted to regurgitate and vomit. Because partial intestinal obstruction was suspected, a gastrointestinal series with iodized oil was done. Subsequent to this, roentgenograms of the skull were found to contain irregular confluent densities in the region of the right middle ear and mastoid areas which the initial survey films had not demonstrated. The infant was discharged as somewhat improved but was followed in the clinic by means of serial roentgenograms. The radiopaque densities were gradually noted to become smaller and less dense. At no time were there any other abnormalities noted in this region nor was anything similar seen on the contralateral side. The child's clinical course was that of cerebral damage due to birth trauma.

From the Department of Radiology and Pediatrics at the Bronx Hospital.

New York Medical College, Flower and Fifth Avenue Hospital (Dr. Chusid).

* References 1 and 2.

Fig. 1—Lateral view of the skull taken Oct. 6, 1952, at 2 days of age, prior to iodized oil swallow. No radiopacities are present in right middle ear and mastoid area.

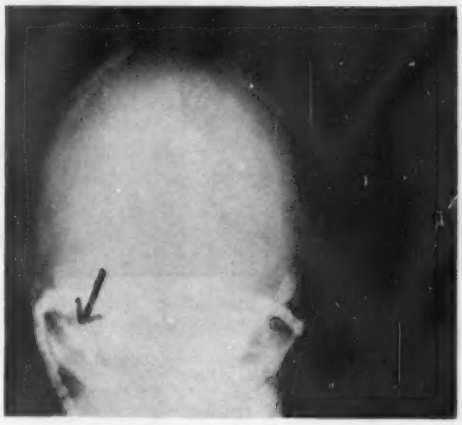

Fig. 2.—Posteroanterior view of the skull on Oct. 10, 1952, showing radiopacity in the region of the right Eustachian tube and middle ear.

Fig. 3.—Lateral view of the skull on the same day.

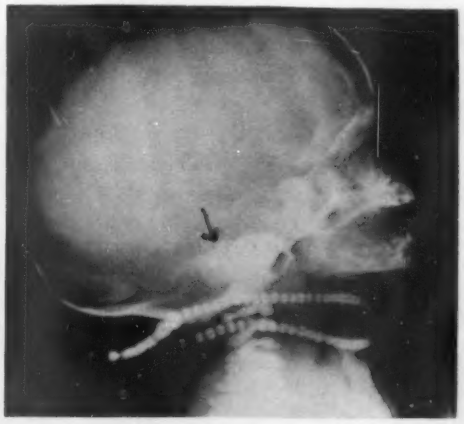

Fig. 4.—The right mastoid on March 4, 1953, showing gradual elimination of the iodized oil.

COMMENT

The presence of radiopaque densities in the region of the right middle ear after a gastrointestinal study with iodized oil, which were not present previously, indicates that this opacity is due to adventitious deposition of the oil in the middle ear via the Eustachian tube. This is gradually being eliminated, and there is no other evident middle ear pathology. It is thought that many cases of tuberculous infections of the middle ear occur through the same route.† Contributory mechanisms may be (*a*) the low surface-tension of the oil and (*b*) a defective swallowing mechanism.[1]

SUMMARY

We present a case of adventitious deposition of iodized oil in the right middle ear following a gastrointestinal series with iodized oil. The oil was deposited in the middle ear via the Eustachian tube. The possibility of adventitious deposition of iodized oil should be entertained when radiopacities are seen in the middle ear region.

Dr. J. Caffey gave suggestions in the preparation of this paper.

† Reference 3 and Caffey, J.: Personal communication to the author.

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Progress in Pediatrics

COMMENTS ON SOCIOPSYCHOLOGICAL ASPECTS OF JUVENILE DELINQUENCY

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and
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A PRELIMINARY estimate from the Children's Bureau puts the number of delinquent children brought to the courts in 1953 at about 435,000.[5] This is a new all-time high. These figures show that there were 13% more juvenile court delinquency cases in 1953 than in 1952 and that juvenile delinquency has risen again for the fifth consecutive year.[5] It seems probable that the final figures will show the increase in delinquency cases for the five-year period 1948-1953 to be somewhere between 45% and 50%.[5] This rise cannot be explained in terms of population growth alone, for during the same period a rise of only 7% occurred in the child population between 10 and 17 years old.[5] To make matters worse, these statistics portray only a small part of the total problem. It has been estimated that about three-fourths of the children who have contact with the police because of some alleged delinquency do not get to juvenile court,* and in any case, there are a great number of delinquent children who escape the attention of the law completely. The number of these "hidden delinquents" is not definitely known, but studies indicate that their sum is considerable.[3]

It is, of course, impossible to estimate truly the cost of juvenile delinquency in this country, and it goes without saying that the most serious damage cannot be measured at all. One cannot begin to assess the cost in personal unhappiness, in wasted and unproductive years, in family distress, and in the many other problems that result when a young person turns to delinquency.[3] However, the cost of public services for helping delinquent children can be measured. The Children's Bureau in 1951 estimated that the average cost to the public for handling each delinquent child was $300.[3] Taking last year's figure of 435,000 children brought to the attention of the juvenile courts, we may reckon that in 1953 this aspect of delinquency cost the public about $130,500,000. This figure does not include the cost of children picked up by the police and then released.[3]

Unfortunately, it seems evident that much of this money was wasted.[3] Studies show that approximately 35% of the young people who come to court have been there before on one or more occasions.[3] In addition, it appears that more than 5 out of every 10 young people who come before our juvenile courts today go on to commit one or more serious crimes for which they will be convicted as adults.[3]

These findings lead to certain conclusions: One is that our agencies for helping children

Director, Department of Child Psychiatry, The Menninger Foundation (Dr. Hirschberg); Chief of the Children's Section, Topeka State Hospital (Dr. Noshpitz).

Dr. Clifford R. Shaw supplied both material and advice for this paper. Dr. Shaw and others in the Chicago Area Project have done much work on the role played by social factors in the etiology of juvenile delinquency.

Read in the Symposium on Emotional Problems of Children as They Contribute to Juvenile Delinquency in the Joint Meeting of the Section on Pediatrics and the Section on Nervous and Mental Diseases at the 103rd Annual Meeting of the American Medical Association, San Francisco, June 25, 1954.

* Beck, B. M.: Community Action to Curb Juvenile Delinquency, address to the Kansas Conference of Social Work, April, 1954.

are inadequate in number. A second is that we do not offer the right kind of service in dealing with the problem of delinquency.[3] It is to this last conclusion particularly that the body of this paper will be addressed.

Although this paper will deal with some of the sociological aspects of delinquency, this limitation should not imply a lessened recognition of the importance of genetic and dynamic determinants in the individual delinquent. But our central thesis here is that there exist two basically different kinds of delinquency. One is that of the individual delinquent whose particular constitution and home background have produced a person with an emotional illness, one of whose symptoms is antisocial behavior. The other kind of delinquency is that of the child without real emotional illness who gets involved in a delinquent group, who behaves antisocially only when in group, and whose delinquent behavior is thus determined by external sociologic forces rather than by internal psychopathology. This latter group comprises by far the largest number of our current crop of "problem children."

Although physicians have always recognized the delinquent as the product of social forces, nevertheless, much of the primary emphasis thus far has been on individualization both in treatment and in prevention.[33] We have thus failed to emphasize that all delinquency is not symptomatic of emotional illness, that certain delinquency emerges from the pressures of group living, and that we cannot consider the delinquent only as an independent unit, but must pay attention to the groups within which he is a participating and reactive member.[33] Further, the psychological problems which account for the "delinquent culture" are not necessarily the same as those which bring about and motivate the individual delinquent.[6]

In certain city areas, "the blighted areas," delinquent groups are a significant part of the social organization.† Delinquency is thus a function of people in places. But what is there in the place which fosters delinquency? Not the land, not the houses, not the physical attributes as such, but the meanings which those things have for people; the limitations they place; the frustrations they engender. The people who live in these areas, regardless of their personal morality, have a strong group sense of rejection by the larger and wealthier society on whose outskirts they live. Tremendous feelings of frustration and resentment ensue, and group attitudes condoning hostility, rebellion, and destructiveness come into being. As a result, a mother and father in such a society may raise their child with the conventional emphasis on honesty, respect for property, etc., while they simultaneously express their bitterness, criticism, and hatred of the larger society with which they struggle. As an individual, the child may have no serious emotional problems. But as a member of a culture, he freely joins with others into an aggressive group capable of antisocial activity. Nor is this problem confined exclusively to the poor. Many people who have struggled hard for years to accumulate a large fortune have powerful wishes for a hedonic way of life which they verbalize but do not act on—but which their children proceed to realize. Wanton indulgence of sexual impulses, of desire for "high living," or of "madcap" activity, may all be values in the parental culture, although as individuals these same parents may be reasonably conventional people. Their group ideal, however, achieves concrete form in the behavior of their children when the latter come together and form a clique, a set, a club, or whatever. Fundamentally the group phenomenon is the same, and the outcome in either case, rich society or poor, is a delinquent group. From the point of view of our society, however, the major problems arise with the groups and gangs that come from the more marginal economic societies.

In a doctoral dissertation, Cohen [6] states:

> Children who share lower class culture and therefore common status problems may gravitate toward one another and form sub-systems within the larger social system. Sub-systems such as a delinquent group, are formed within which those characteristics which stigmatize them in the light of middle class norms are precisely those which now confer

† References 26, 27, and 29.

status. This leads to an exaggeration and intensification of all the features of the "corner boy" described by Whyte,[36] especially of those which contrast most with the "college boy" pattern. Indifference to school and distrust of middle class authorities is already present in the lower class culture. In the type of response here described indifference and distrust are converted to the positive virtues of open defiance and aggression. Behavior then is not an obscurely displaced aggression. It is a direct assault upon the source of frustration, upon the kind of people who look down upon you, either because of your family background, or because you don't have the kind of personality interests and goals that they approve of.

In such a group, a boy's motivations for delinquent practices are similar to the motivations of adults whose activities meet with the approval of the total community.[2] Thus, one sees delinquency emerge from the dynamic life of such societies.‡ The delinquent practices of these youngsters are as vital to them in serving their immediate personal and social needs as are the approved forms of conduct to children residing in the more conventional community areas.[2] The group delinquency represents a struggle for adjustment.

Let us examine the relation of the group delinquent to his group in some detail. First, any child uses the group for the achievement of recognition and status.[2] In the delinquent group, however, prestige and pride are derived from antisocial acts, from long records of delinquency, and from time spent in correctional institutions rather than from conformity to the standards of conventional society.[2]

Second, any child uses the group to express instinctual impulses which the group structure permits.[25] In the delinquent group, aggressive drives can be expressed within the group, both through rivalry and competition, and externally, through the group attitude toward authority, an attitude of overt hostility which can lead to direct acts.[6] Further, the delinquent group is used by its members to help deal with many of the conflicts centering around masculinity-femininity struggles.[31] This is not only seen in the actual heterosexual activity of some group members, but can also be found in the gratification derived from the symbolic meaning of many delinquent acts.[2]

Third, the delinquent uses the delinquent group just as the adolescent in any society uses his equals to formulate values and patterns for behavior.[27] In his struggles for emancipation from his parents, the adolescent in our culture often temporarily more or less isolates himself from his family and from their standards. During this time, he seeks from his peers the understanding, the sympathy, and the shared awareness which he previously sought from his family. The normal adolescent groups which result have their own rules of conduct, their own ideals, and their own heroes to worship. They exercise independent control over their individual members and offer security to each of the members in the sense of belonging to the group as a whole. All of these factors apply to the delinquent group just as they apply to the normal group. The crucial difference, however, is this: in the delinquent group, delinquent behavior itself is an objective or a goal,[2] whereas in the normal group conformity to the standards of society as a whole is the usual objective. For the individual child, delinquent behavior represents conformity to the expectations of the delinquent group, just as socially acceptable behavior represents conformity to the expectations of the normal group.[2]

Many studies indicate that delinquency in blighted areas is largely molded by community forces that are directly related to the whole social world in which the person lives.§ We can regard the social structure in such neighborhoods as literally demoralizing, and we do not need to assume that the delinquency reflects any biological inferiority among those who live within the areas.[2]

Once a high rate of delinquency becomes a characteristic of such an area, it persists despite successive changes in nationality composition. When certain delinquency areas in Chicago were occupied earlier by German, English, Irish, and French immigrants, the rates of delinquency were uniformly high as contrasted with other neighborhoods of higher economic status within Chicago.

‡ References 2, 27, and 28.

§ References 2, 25, and 26-29; Shaw, C. R.: Personal communication to the authors.

Further the rate of delinquency among these early immigrant groups markedly decreased as they prospered and moved to more desirable localities, while the high rate persisted in the areas from which they moved. As the Scandinavian, Polish, and Italian populations succeeded these others in the deteriorated areas, large percentages of children from these groups irrespective of nationality, began to come to the attention of the police and the courts.[2]

Thus, to understand the total problem of juvenile delinquency, we must examine the problem in its two aspects.[25] First, from our understanding of the individual delinquent whose family background promotes the expression of emotional conflict in socially unacceptable ways, and second, from our knowledge of the group delinquent whose adolescence takes place under such social and community conditions that he has small chance to achieve a normal resolution of his dependency and masculinity-femininity conflicts without using the delinquent group. In this second group, the group delinquents, we see that the psychopathological defenses that bring about delinquent behavior develop as a response to the social milieu.

Let us regard the issue theoretically. One way of conceptualizing the psychopathology of delinquency is to define it in terms of conscience defects. We can explain the antisocial behavior by postulating conscience defects that permit the delinquent to act out his impulses in antisocial ways without hindrance from within himself. Of basic importance, however, is how these conscience defects come into being. In general, conscience is formed by a taking in of the social milieu (including family) in which the child is reared. If we consider a culture other than our own, it is easier to see how social structure plays a role in the development of conscience. For example, a youngster growing up in a gypsy society might have certain values and standards about stealing which would be very different from those of the villagers among whom he wanders. He would have incorporated a conscience which was "defective" in at least one area, in that it held stealing to be an acceptable way of obtaining money. This would be both his family's teaching and the way of the group. Once having incorporated the values and images of his parents and his culture, this gypsy youngster would then not only be able to steal without conflict, but would steal as an activity of his sociological group. There would be no conscience pressure brought to bear on him when he stole. Nor would he have guilt about what he did. Stealing would be an easy and natural act. On the other hand, he might have a good deal of fear of reprisal and he might experience much reality-based anxiety in connection with his act. But it is important to realize that the conflict he experienced would be a conflict between himself and external reality, not between him and his own conscience. Thus, both the individual family traits and the social milieu in which this gypsy child developed would serve to provide certain controls and at the same time to allow channels in the control system through which internal impulses could find expression, channels which, viewed from another sociological base, would be considered as delinquent activity.

Now if we observe the personality development of a child within our own culture from a longitudinal standpoint, we note that there is normally a growth of the impulses and wishes of the child on the one hand, and a simultaneous development of the child's mastery and control over these impulses on the other. The number and strength of the impulses develop along with the maturation of the body, and the control over these impulses grows as the child's capacity for learning and for relating to others increases. Significantly, however, progress in the growth of these two elements of personality structure is not always uniform. Thus it is that at about 4 or 5 years of age pressures of the impulses pose quite a problem to the child, and the child solves this problem by turning to the immediate external environment, the parents, in order to draw strength from them. This is the time when conscience undergoes great growth, as the child identifies with and internalizes his parents in order to increase his own ability to

master and control. For the gypsy child, or the child of criminal parents, the "conscience" that is formed at this time is likely to be grossly defective, and we have the most serious kind of "individual" delinquent to cope with later on. In most cases, the situation is not so extreme, and the conscience that results is only partially defective. Such a youngster may well be emotionally ill with constant strife both within himself and with society. In the normal child, after the identification with the parents has taken place, the now strengthened control system allows him to enter the grade school years, a time distinguished by increasing development of academic learning, physical mastery, and technical skills, with less marked growth of the instinctual impulses. This equilibrium persists until puberty, when the physiological changes of adolescence cause an increase in the pressure of the instinctual impulses. Again, the child's control and mastery is beset by powerful instinctual pressures, and again the personality must cast about for some means of strengthening its control forces. Once more, identification and identity formation become the instruments of choice. In adolescence, however, the previous sources of strength to the child (the parents) are not usable in the same way as they were to the 4- and 5-year-old. The sexualized and aggressive impulses that are so characteristic of adolescence at once make the previous intense bond to the parents now "too hot to handle." Aggressive wishes and sexual impulses toward the parents are unthinkable now that the child's body is sexually fertile and physically much more powerful. Parents become the one group to whom many an adolescent cannot address himself, and thus the youngster begins to seek identity patterns away from home in the larger social milieu. With the "loss of the parents," the adolescent faces a problem both difficult and frightening, the problem of being alone and bereft. He now desperately seeks security in new identification figures, and the most ready source for such figures are his adolescent peers. These are the people who both share his problems and can also be the objects of his impulses. And so, the adolescent group is born and, for a while, plays a crucial role in the development of the personality of its members.

It seems then that the nature of the groups which become available at this point can determine both the immediate behavior and even some of the lasting identifications of the group members. However, as we observed before, the manners, the mores, the values, the leadership of these adolescent groups are functions of the larger social setting within which the group appears. They represent the group attitudes of their society, the attitudes which might love a Robin Hood while hating theft and encourage stealing from big companies while deploring pickpockets. These groups then become one of the most direct channels by which the social milieu impinges on the behavior patterns and the personality growth of its youngsters. In those social organizations which lead to adolescent groups of an antisocial cast, the various members of the delinquent group will be modified both by the identifications thus formed and the actual events that ensue. Once a "delinquent culture" has been established, specific persons may participate in it for different and individualistic reasons.[6] If a boy with a relatively intact conscience shares in the stealing adventures of a group merely as part of the group, several possibilities are open. He may grow up without further complications and remember these escapades with mixed feelings. On the other hand he may get caught and brought to trial. If he then gets sent to the penitentiary, he may emerge with antisocial attitudes due to his new identity as an injured person who deserves revenge. Thus he would be quite different from a person who originally had a defective conscience and who would have stolen with or without the group or with or without penitentiary experience.

The search for identity, however, is not exclusively bound to the adolescent group. The adolescent's bonds to people, once detached from the parents, may also seek sub-

stitute adults, warily and distantly perhaps, but nonetheless pressingly. Somewhere, on some level, the youngster must employ some adult figures to "teach" him how to be, how to act, what to strive for, and how to solve his problems. Again the nature of the available opportunities within the social organization is often crucial in determining who will be selected as the particular youth's choice. It is a characteristic of the adolescent period that a certain amount of experimentation ensues; the youngster must try on and discard various identities, sometimes in rapid sequence, in an attempt to find one that "fits." The "fit" will depend on how well the particular character pattern chosen will be consonant with the demands of the impulses, the pressures of the conscience, and the nature of the social reality with which the individual child must cope. In a search for ways to get along in a world where parents are for a period of time relatively useless, most children will often make a temporary exploration into some kind of antisocial behavior, gaining their cue from available models and particularly from group models. On the other hand, many children in deprived city areas not only explore, but adopt antisocial behavior as a mode of living, when the social organization supports and maintains these values. Hence the socially derived identifications of the adolescent, added to those identifications of family origin, determine the nature and quality of the adolescent's relationship to society itself.

It is likely that participation in the "delinquent group" is facilitated by family relationships which have been lacking in strong affectional ties between the parents and the children in the early years of childhood or lacking in parental restraints and controls, and it may well be that within the lower socioeconomic classes this aspect of family relationships is one of the differentia between families of delinquents and nondelinquents within the same social organization.[6] Further, defects within the family may be responsible at least in part for both the marginal conditions of living and the juvenile delinquency.[13] Certainly a deterioration in family values would result in a loss of the personal integrity and the loyalties upon which stable relationships are based. However, we must abandon the belief that all juvenile delinquency is a consequence of personal inadequacies in a culture that is essentially adequate,‖ and we must recognize that more than therapy for the individual child is needed in order to prevent or remedy delinquency that emerges from pressures of group living.[33]

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CAUSES OF JUVENILE DELINQUENCY

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DATA ON the frequency of juvenile delinquency are necessarily inaccurate. Prominent among the uncontrollable variables are different laws in different states, changing laws in the same state, the vigilance and adequacy of the police force, and the attitude of the police and the courts. Nevertheless, according to the best available sources, juvenile delinquency is increasing in the U. S.

It is worthy of note that delinquency is prevalent despite an improvement in the general economic level, better housing, extensive slum clearance, more play facilities, and a wider application of psychiatric knowledge.

PERSONALITY AND BEHAVIOR OF THE DELINQUENT BOY

A composite picture of the type of youngster who becomes delinquent has been presented by Drs. Sheldon and Eleanor Glueck.[1] Their observations were based on a comparative study of 500 delinquent and 500 non-delinquent boys varying in age from 11 to 17 years. The individual boys were matched for age, ethnic origin, and general intelligence. The children of both categories were from low economic groups and resided in an underprivileged neighborhood in Boston.

A striking fact brought out by these studies is the early age at which delinquents begin to get into trouble. Many were already in difficulties while in kindergarten or first grade for such complaints as disobedience, unruliness, defiance, stubbornness, temper tantrums. By the time they were 8 years old nearly half of the delinquents studied by the Boston workers were in some trouble and another two-fifths were involved before their 11th year. Although normal boys frequently commit minor transgressions such as hopping trucks, petty pilfering, occasional truancy, and smoking, delinquents generally give a history of persistent and serious misbehavior such as burglary, various forms of larceny, automobile theft, crimes against the public order, running away, truancy, assault and battery, and the like. Court appearances and convictions take place early, on the average at 12.4 years, and are repeated.

The emotional attitudes of the lawbreakers are characterized by hostility, defiance, resentfulness, suspiciousness, and social assertiveness. A prominent characteristic is a strong feeling of not being appreciated. Delinquents have an intense desire for power and position but at the same time they tend to be parasitic and want to be looked after. By and large they are uncooperative, unconventional, resistant to authority, independent, and uninhibited. Additional traits are stubbornness, egocentricity, lack of self-criticism and sensuality.

Their relationships with other members of their families, with members of the opposite sex, and with society as a whole are less satisfactory than those of law-abiding boys. They often express their inner conflicts in

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action or emotional outbursts rather than by suppressing them as do other persons. They seem to suffer less than others from such emotional reactions as anxiety, feelings of insecurity, helplessness and powerlessness, and fear of failure and defeat. Taken by and large the delinquent is a dissatisfied person.

At school the work of the delinquent boys is, in general, poorer than would be expected from their intelligence level. They are, on the whole, uninterested, inattentive, careless, and lazy, and they are often left behind. Formal training of any kind is resented, and little thought is given to planning for the future. For after-school jobs they prefer street trades such as peddling, boot blacking, and selling newspapers and less often jobs where they are subject to a certain amount of supervision and protection such as office work or store help.

For amusements delinquent boys generally seek adventurous activities rather than competitive sports or games or quiet pursuits. Favorites are stealing rides, hopping trucks, roaming the streets after dark, smoking and drinking at an early age, destructive mischief, running away, firesetting, and gambling.

This, then, is the sort of youngster who becomes delinquent. What are the forces which make him become a law breaker?

PHYSICAL AND MENTAL HEALTH

Physical health may be ruled out as a factor of significance. The Gluecks found that, as a group, the delinquent boys have better musculature and are more masculine than nondelinquents. They show bodily disproportions less frequently.

Mental health, similarly, does not seem to be an important consideration. According to the findings of the Gluecks, again, psychiatric disorders—psychosis, psychopathy, psychoneurosis, neurosis—are no more frequent among youthful transgressors than among controls. Bovet,[3] in a report for the World Health Organization, came to a similar conclusion.

Moreover, an attempt to prevent delinquency in children through psychotherapy of a "predelinquent" group of boys, 6 to 10 years of age, proved unsuccessful.[4] Actually, the incidence of delinquency was a little higher in the treated than in the untreated control group.

This is not to say that the psychiatrist has no function, or even only a minor one, in the problem of youthful transgression. Though the forces which motivate the juvenile delinquent are not in themselves pathological, these forces are nevertheless subject to study, and the psychiatrist should serve a useful purpose here. Moreover, the fact that psychotherapy, as currently practiced, has been found ineffective in preventing delinquent behavior does not mean that some other psychotherapeutic approach might not be effective.

Feeble-mindedness is somewhat more frequent in delinquents than in the general population. This is accounted for, in part at least, by the likelihood that the defective will be more readily apprehended than the brighter boys. However, the percentage of mental defectives that are delinquent is small. The I. Q. of lawbreakers is not far below the average for the population as a whole.

A study of the relation of reading disability to juvenile delinquency has been carried out in New York City under the direction of Dr. Harris Peck.[5] A survey in 1951 revealed that 76% of the lawbreakers were retarded two or more years in reading. Half of these were retarded five or more years. The incidence of reading disability in school children in general is about 10%.

The authors attribute much of the reading difficulty to a deficiency in preschool readiness experience, many of the children coming from homes where a foreign language is spoken and where verbal communication is on a primitive level, so that interest in language skills is minimal. The books and material used in the schools have little meaning for youngsters with such a background. Moreover, with overcrowding in the schools,

teachers are limited in their ability to give individual attention.

SOCIAL FACTORS

Economic Status.—Poverty is not a prominent factor producing juvenile delinquency; nor does prosperity reduce lawbreaking. Though the delinquency rate rose somewhat during the depression years of the early 1930's, it rose much more sharply and to a much higher level than ever before in 1943 and has continued to increase ever since. According to Reinemann,[6] delinquency is highest during periods of extreme prosperity.

Juvenile delinquency is no longer a product of the slum areas. It has spread to the more prosperous sections of the community and to the less densely populated areas of the country.

Improved housing has not reduced the frequency of juvenile misbehavior. Extensive slum clearance since the war has been without beneficial effect. Lander,[7] whose study was made in Baltimore, concluded that substandard housing bears no causal relation to juvenile delinquency. On the other hand, home ownership, which he regards as a stabilizing influence, acts as a deterrent to juvenile lawbreaking.

Nor have increased playgrounds—in New York City, for example—helped to reduce juvenile misbehavior. Tappan[8] concludes that recreational activities are valueless as deterrents to crime.

A prominent place in the etiology of delinquency has been attributed to membership in gangs. The data do not bear this out. It is true that over half the lawbreakers in the Glueck's study group belonged to gangs, in contrast to only 0.6% of the nondelinquents, but the delinquents had revealed their antisocial behavior long before they became gang members. "Gang membership may multiply antisocial activities; it rarely originates persistent delinquency."[1]

Race and Ethnic Origin.—According to the 1903 Federal Slum Survey, juvenile delinquency was concentrated in areas populated by the foreign-born. By 1940 the situation had changed and youthful lawbreaking had become a characteristic of areas inhabited by the native-born. Two ethnic groups—the Chinese and the Jews—show very little delinquency.

Juvenile delinquency is commoner among Negro than among white children. In the Baltimore study made by Lander[7] the incidence was two and a half times as great as among whites. However, the Negro rates varied widely in different areas in the city just as did the white rates, which means than race alone cannot account for the difference in behavior. The Negro rates were highest in areas with admixtures of white population and lowest in areas which were almost exclusively Negro. In fact, in areas with the highest proportions of Negroes the Negro rate was no higher than in similar areas of total white occupancy.

Lander regards his data as amply demonstrating that the greater over-all incidence of delinquency among Negroes is not related to race as such but rather to social instability.

A factor often considered important in bringing about delinquent behavior is a conflict between a foreign culture of the parents and their American-born sons. This was found to be of no influence by the Gluecks, the proportion of foreign-born parents being the same in delinquent and nondelinquent groups.

Dr. Richard Cabot, whose eminence as a professor of social ethics paralleled his position in the medical world, suggested that the predelinquent boy needed an adult "friend" who would stand by him through thick and thin—he needed some one who would make available to him the opportunities and moral guidance that parents normally supply. This hypothesis was tested by Powers and Witmer[9] and found to be effective only occasionally in preventing future misbehavior.

Concern and uncertainty about the current world turmoil is not a direct consideration. Most of the youthful lawbreakers take little interest in political or foreign affairs and are hardly aware of the world situation.

The available data indicate, then, that many of the conditions popularly regarded as producing delinquency have little or no influence. Let me say however that, although these factors have no over-all significance for the problem of delinquency, they may be crucial in individual instances. For example, without question certain delinquent acts are manifestations of epilepsy or psychosis; in others poverty is the determining factor, and in certain groups, the glut of wealth, but by and large the proportion of such cases is small.

We come now to a consideration of factors which probably do bear a causal relation to delinquency.

FAMILY BACKGROUND

An unstable home is a potent factor in the production of juvenile delinquency. By and large the families of youthful lawbreakers are less satisfactory than those of nondelinquents from the same socioeconomic environment. The homes are frequently broken by separation, divorce, death, or prolonged absence of one or both parents. Emotional disturbances, feeblemindedness, alcoholism and criminal behavior are frequent among the parents. On the whole they lack self respect, are less ambitious for themselves and their offspring, and set poor examples for their children. A warm relationship between parents and child is unusual. The mothers show little interest in their children. They tend to be lax and inconsistent in their disciplinary attitudes. On the other hand, the fathers are generally overly strict and resort to physical punishment readily. The families move about frequently, and so the children have little opportunity to make neighborhood friendships.

In general the picture presented by the parents is one of little understanding, affection, stability, or moral fiber. They may be characterized as generally unfit to be proper guides and protectors or suitable models for their children.

On the other hand, delinquency sometimes arises in homes which seem in every way ideal.

PERSONALITY

By no means all the children reared in inferior homes are delinquents. Indeed, the proportion is relatively small. Certain children seem to be especially susceptible to influences leading to delinquency. Among the characteristics mentioned by the Gluecks are a temperament which is restlessly energetic, impulsive, extroverted, aggressive, and destructive; an attitude which is hostile, defiant, resentful, suspicious, stubborn, socially assertive, adventurous, unconventional, and nonsubmissive or ambivalent to authority, and intellect which tends to direct and concrete rather than symbolic and abstract expression and which lacks a methodical approach to problems.

INEFFECTIVENESS OF DETERRING FORCES

Juvenile delinquency may be regarded as a resultant of motivating and deterring forces. It is Tappan's view [8] that an important factor in the increase of juvenile delinquency is the dwindling ability of home, church, and community to deter young people from behaving in an antisocial manner. As moral and social forces lose their influence, responsibility for control has passed to the state and its courts. These are not sufficiently strong to curb lawless behavior.

Mr. J. Edgar Hoover [10] says in this relation:

> Juvenile delinquency is a reflection of the moral tone of the nation. Young people can't be expected to behave if their elders don't. A society which produces a high incidence of divorces, broken homes, illegitimate births and adult crime creates juvenile misbehavior. Remedial action can only come from a renewal of civic responsibility. This responsibility must start in the home. There is no alternative.

Of primary importance in the production of juvenile delinquency is the social setting. A society in which young people are led to believe that to have fun is the primary aim of life, a society in which moral restraint and personal responsibility are minimized, a society in which authority—parental, religious, community—is flaunted breeds delinquency.

CONTRIBUTING FACTORS

Newspaper Publicity.—The desire to be in the limelight, to be prominent, to be a big shot is a strong motivating force in many youngsters. The urge to achieve and to succeed in one's chosen field is laudable, but the aim must be worthy and the means honest and aboveboard. Unfortunately, misdeeds are publicized and glamorized in the popular press to such a degree that they are used to get publicity. This may be a more important consideration than we appreciate. The Gluecks emphasize a desire for power and position as being strong in delinquents. A prominent New York daily recently carried on its front page the picture of a young man embracing his bride. The reason for the spread was that the young man had struck his prospective mother-in-law because she had presumed to object to her daughter's choice. Such publicity, by glorifying the crime and the youthful criminal, serves to encourage transgression. Instead, measures which would treat delinquent behavior as the cheap, mean, petty, cowardly behavior which it actually is might well, by humiliating the transgressor in the public eye, discourage delinquency.

Prolonged Schooling.—Another consideration is the undue prolongation of the schooling period for the large number of adolescents who are not book learners. Such youngsters find the school a bore. They learn nothing themselves and they interfere with the progress of the more studious ones. Nevertheless, they cannot leave school because of compulsory school laws.

These boys have a disrupting influence on the school activities. They clown in the classroom, and they ridicule and threaten the industrious students. Agnes E. Meyer [11] points out that

> delinquency is as contagious as measles and ten times more dangerous to the health of the student body. The code that prevails in the large schools is not that of the good boys but that of the desperadoes.

The situation in the schools has reached the point where a special committee on delinquency, appointed by the Superintendent of Schools in New York,[12] has recommended that the law on compulsory school attendance be amended to permit 16-year-olds to quit school and that the law be made flexible to allow 15-year-olds to work. Other recommendations were that provision be made for protection of the school from juvenile vandalism, that parents be expected to assume their due responsibility toward the youngsters' performance and behavior at school, that there be more classes for retarded children, and that the programs for remedial reading and arithmetic be extended.

SUMMARY

A number of conditions, widely regarded as producing juvenile delinquency, have been shown to have little or no over-all influence. Such conditions are poverty, inadequate housing, inadequate play facilities, cultural conflict between the foreign-born parent and his native-born child, lack of a supporting figure whom the boy could model himself after, membership in gangs, and physical or mental abnormality.

The forces which produce delinquency are to be found in an inadequate family background, a type of personality, the social setting, and a general relaxation of the restraining influences of home, church, community, and state.

Contributing factors are the undue publicity given the delinquent by the popular press, the prolonged schooling of boys who are unwilling or unable to profit by book-learning, and the social instability in areas where racial groups clash.

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Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

TOTAL BODY CHLORIDE OF CHILDREN IN POTASSIUM DEFICIENCY AND UNDER CIRCUMSTANCES OF POOR NUTRITION. DONALD B. CHEEK, Pediatrics **14**:193 (Sept.) 1954.

The distribution of bromide has been used to measure total body chloride in children of poor nutritional status and in circumstances of potassium deficiency.

In malnutrition there is an increase of extracellular water and of tissue chloride per unit weight.

One patient with fibrocystic diseases revealed a deficit of body chloride during heat stress.

Children with chronic gastroenteritis and potassium deficiency receiving only glucose and saline tend to develop chloride and water retention in the extracellular compartment. It is not known whether potassium deficiency per se is causally related in this finding.

Deficits of extracellular sodium and of chloride have been revealed in four cases of hypotonic dehydration with cell potassium deficiency. Presumptive evidence only of potassium loss was presented in one case of pyloric stenosis, but conclusive proof was offered in the investigation of a child with acrodynia.

FROM THE AUTHOR'S SUMMARY.

AMINO ACIDURIA AND ASCORBIC ACID DEFICIENCY. J. H. P. JONXIS and T. H. J. HUISMAN, Pediatrics **14**:238 (Sept.) 1954.

In two cases of infantile scurvy, an increased output of amino acids was found which disappeared during three or more weeks of ascorbic acid administration. The excretion of threonine, serine, glycine, tyrosine, histidine, lysine, and β-aminoisobutyric acid was increased, that of the other amino acids being normal. Plasma ultrafiltrates from two scorbutic infants were found to contain amino acids in similar concentrations to those of two control infants. The aminoaciduria of scurvy is thus apparently of renal origin.

FROM THE AUTHORS' SUMMARY.

NITROGEN BALANCES ON LOW NITROGEN INTAKES IN INFANTS AND THE EFFECTS OF GELATIN SUPPLEMENTATION WITH AND WITHOUT VITAMIN B_{12} AND AUREOMYCIN. ROBERT KAYE, RONALD H. CAUGHEY, and WALLACE W. MCCRORY, Pediatrics **14**:305 (Oct.) 1954.

A group of five boy babies who received an average nitrogen intake of 98 mg/kg/day, derived from cow's milk protein, retained an average of —2.0 mg/kg/day. Small positive balances were achieved at intakes of 110 mg/kg/day in two subjects. An intake of 100 mg/kg/day in two subjects resulted in one instance of nitrogen equilibrium and one of negative nitrogen balance. In the subject given the lowest nitrogen intake, 70 mg/kg/day, a negative nitrogen balance was encountered. These data suggest that the lower limit of nitrogen intake for equilibrium in infants under the experimental conditions reported here is approximately 110 mg/kg/day.

Two of these subjects received gelatin supplements providing 120 mg of N per kilogram per day and responded with increased nitrogen retentions of 50 and 60 mg. of N per kilogram per day.

Retention of the gelatin supplements was not further increased in either subject by the administration of 300γ of vitamin B_{12} and 200-300 mg. of chlortetracycline (Aureomycin) daily.

The provision of a protein which does not contain all of the essential amino acids as a supplement to protein of good biological quality permits real augmentation of nitrogen retention.

Certain implications of the data in regard to the nutritional value of suboptimal intakes of nitrogen and total Calories have been discussed.

FROM THE AUTHORS' SUMMARY.

THE RESPONSE OF INFANTS TO A LARGE DOSE OF WATER. R. A. MCCANCE, N. J. B. NAYLOR, and E. M. WIDDOWSON, Arch. Dis. Childhood **29**:104 (April) 1954.

After a test dose of water equal to about 6% of the weight of water in the body, infants aged 6-18 days (1) rapidly increased their urine volumes till they were similar in magnitude to those of adults per unit of body water or per unit of water administered; (2) passed urines at the

peak of the diuresis as dilute as those passed by adults; (3) did not (as adults did) excrete a volume of urine equal to that of the test dose within four to four and a half hours; (4) had glomerular filtration rates nearly equal to those of adults per unit of body water and treated the filtrate in the same way in its passage down the tubules. There was no evidence that a change in minute volume was brought about by a change in glomerular filtration rate.

KELLY, Milwaukee.

ESTIMATION OF CALORIC NEED IN ATROPHIC INFANTS. L. KULIN, Ann. pædiat. **183**:162 (Sept.) 1954.

The usual calculations of Calories according to weights or measurements have proved unsatisfactory in atrophic infants. As these decomposed infants are unable to gain weight in their "cold milieu" of 22 C, it has been impossible to assess their requirements empirically. The author thought that food supply should be in relation to the active body protoplasm. During atrophy, the inactive body substance has been lost partially or totally, and it is therefore necessary to consider the relation of active to inactive body substance in these cases. The correctness of this assumption has been proved in the climatic ward: in spite of lowered requirements of Calories on account of the humid-warm climate it was found that the atrophic infants still require from 10%-30% more Calories according to the relative loss of inactive body substance per kilogram of the original body weight. The optional requirements in about 75% of the atrophic infants were 130-150 Cal/kg.

The enormous alimentary capacity of the active protoplasm was shown in 5% of the infants nursed in the climatic ward who only gained satisfactorily on a supply of 160-180 Cal. It was found under the same conditions that the maintenance requirements of the atrophic children were near 100 Cal/kg. and not 70-80 Cal.

The author found that the ideal climatic milieu for atrophic children should have a temperature of 28-30 C (82.2-86 F) and a relative humidity of 55%-70%. At room temperature the atrophic organism is forced to utilize the food for heating purposes instead of for body building.

FROM THE AUTHOR'S SUMMARY.

Hygiene; Growth and Nutrition; Public Health

COMPARISON OF GROWTH IN HEIGHT AND WEIGHT BETWEEN ECTOMORPHIC AND MESOMORPHIC BOYS. C. WESLEY DUPERTUIS and NANCY B. MICHAEL, Child Developm. **24**:203 (Sept.-Dec.) 1953.

From a somatotype study of 125 young men, 26 ectomorphs and 28 mesomorphs were selected for a comparative study of their physical growth as indicated by measures of height and weight from 2 to 17 years of age. At the time they were somatotyped, both groups averaged about 21 years of age, and the ectomorphs averaged 2 3/10 in. (5.8 cm.) taller and 26 7/10 lb. (12.2 kg.) lighter in weight than the mesomorphs.

The results of the study showed that from 4 to 17 years of age the ectomorphs averaged consistently taller than the mesomorphs. The mesomorphs, however, averaged significantly heavier, both absolutely and relatively, than the ectomorphs at each age from 2 to 17 years.

A comparison of the growth curves showed that the mesomorphs reached their peak in puberal spurt in both height and weight, on the average, about one year earlier than the ectomorphs.

The ectomorphs were found to grow in height over a longer period of time than the mesomorphs.

The mesomorphs appeared to grow faster, in that they consistently attained a higher percentage of their adult stature at each age level as compared with the ectomorphs.

The conclusions are that the somatotype as indicated by measures of height and weight remains fairly constant, at least for ectomorphs and mesomorphs, throughout childhood and well on into the young adult period. Since growth patterns for boys of contrasting body build are shown to be different, this finding indicates the desirability of further study of growth patterns in childhood of different body types to open the way for more comprehensive research into the problems of individual growth and development.

FROM THE AUTHORS' SUMMARY.

SEASONAL VARIATIONS IN PHYSIOLOGICAL FUNCTIONS DURING ADOLESCENCE. JOHN P. MCKEE and DOROTHY H. EICHORN, Child Developm. **24**:225 (Sept.-Dec.) 1953.

We have examined B. M. R., oral body temperature, basal pulse rate, respiratory rate, and systolic blood pressure for evidence of seasonal variation during adolescence. We find fairly clear evidence of a fall in B. M. R. and pulse rate during the spring, followed by a rise during the autumn. Tentative evidence of an opposite change in body temperature in boys, but not in girls, has been reported.

FROM THE AUTHORS' SUMMARY.

COMPARISON OF SKELETAL MATURATION WITH DENTAL STATUS IN JAPANESE CHILDREN. WATURU W. SUTOW, TARO TERASAKI, and KENJI OHWADA, Pediatrics **14**:327 (Oct.) 1954.

Data obtained from simultaneous skeletal maturation assessments and dental status evaluations of each of 1,360 Japanese children (678 boys and 682 girls) ranging in age from 6 to 14 years have been presented.

Statistically significant differences in number of permanent teeth were demonstrated between the skeletally above-average and skeletally below-average children, skeletally advanced children having the greater number of teeth. At individual age levels, consistent significant differences were not found.

Comparisons of the terminal (extreme) segments indicated statistically demonstrable differences in a greater number of individual age groups, especially among girls.

At each age level, the girls had a greater mean number of erupted permanent teeth than the boys.

FROM THE AUTHORS' SUMMARY.

STUDENT INJURIES IN SECONDARY SCHOOLS IN OREGON. FRANK B. HAAR and DON B. MARTIN, Res. Quart. **24**:276 (Oct.) 1953.

This investigation was instigated for the purpose of analyzing the injuries occurring to students of the secondary schools of Oregon who were insured by the Student Mutual Benefit Plan during the 1948-49 school year. The results were as follows.

Of the 28,878 insured students in this study, 1,815 injuries were reported, which constituted an injury ratio of 6.2 per 100 insured students.

The time of day accounting for the greatest number of injuries was from 3 p. m. to 4 p. m., or 14.5% of the total injuries.

Although injuries occurring during the months of the school year were rather evenly distributed, the month of February was found to have the greatest number of injuries, with 13.3% of the total.

Physical education classes, with 52.9% of the total injuries, more than doubled all other organized and unorganized school activities combined. Others in order of frequency were school building, 13.8%; school grounds, 7.7%; shop, 6.3%; to and from school, 5.2%; classroom, 3.6%; noon-hour activities, 3.3%; extracurricular activities, 2.3%; intramurals, 2.0%, and dressing room and showers, 1.7%.

Sprains, accounting for 31.3% of the total injuries, were the most common type of injury. Contusions were second, accounting for 24.5%. Fractures and lacerations were responsible for 13.3 and 12.6%, respectively. Other frequent types of injuries were infections, 4.6%; strains, 3.3%; abrasions, 3.0%; foreign objects in the eye, 2.1%; dislocations, 2.0%, and hematomas, 1.4%. Concussions, sacroiliac slips, and miscellaneous injuries not otherwise classified accounted for the remaining 1.8% of the total injuries.

Ankles accounted for the greatest number of sprains, with 33.1% of the total injuries. The fingers accounted for 17.7% of the sprains, and the back, 13.2% of the total sprains. The fingers, accounting for 19.1% of the total injuries, were the most frequently injured part of the body. The ankles and the back, with 11.6 and 8.6% of the injuries, were the next most frequently injured parts of the body.

The region of the upper extremities, accounting for 38.5% of the total injuries, was the part of the body most frequently injured. The lower extremities were second, with 30.6% of the total. The head and neck and the trunk regions were responsible for 18.3 and 12.6% of the total injuries.

It was found that 2.4% of the insured students had injuries affecting the upper extremities. There were 1.9 injuries per 100 insured pupils in the lower extremity region. The head and neck accounted for 1.2 per 100, while the trunk had 0.7 injuries per 100 insured students.

FROM THE AUTHORS' SUMMARY.

AN EVALUATION OF THE SKELETAL AGE IN DYSTROPHIC CHILDREN. P. BRUSA and P. MENGHI, Minerva pediat. **6**:649 (Aug. 31) 1954.

Twenty-three dystrophic infants, 4 to 24 months of age, were classified according to their chronological, statural, weight, and skeletal ages. The skeletal ages of 12 of the infants were significantly below their chronological ages; most of these 12 infants were dystrophic by reason of infections rather than of their nutrition.

HIGGINS, Boston.

THE SKELETAL AGE OF CHILDREN WITH CONGENITAL HEART PATHOLOGY. P. MENGHI and P. BRUSA, Minerva pediat. **6**:651 (Aug. 31) 1954.

Practically all of 22 children with congenital malformation of the heart (17 with cyanosis) had a lower skeletal than chronological age. However, their weights and heights were not necessarily lower than normal for their chronological ages.

HIGGINS, Boston.

RECORD OF MEETING FOR PROTECTION OF INFANCY IN BRAZZOVILLE. ANGEL BALLABUGA, Rev. españ. pediat. **10**:95-108 (Jan.-Feb.) 1954.

This is an interesting discussion of some of the activities of W. H. O. and Unesco in French Equatorial Africa and the Belgian Congo. The author lists social and medical problems under the usual names, such as malaria, bilharzioma, oncocercosis toxoplasmosis, tuberculosis, and congenital malformations and lastly reveals to us that juvenile vagabondage and delinquency is very common in rural Africa and suggests some methods for its study and prevention.

ALLEN, Santa Fe, N. Mex.

INFANT MORTALITY. HERNAN ROMERO, ERNESTO MEDINA, and JERJES VILDOSOLA, Rev. chilena pediat. **25**:175 (April) 1954.

Infant mortality represents a measure of the civic and sanitary culture of a nation and is very sensitive to the economic, social, and political phenomena that they suffer, having thus a decisive influence over the expectation of life of its inhabitants.

Infant mortality is studied in Chile, and its high index reflects the precarious state of public health, which contrasts with the faithfulness and honesty of the national statistics. In the present century, the curve is particularly analyzed, showing the factors which have influenced it in different times.

The curves of neonatal mortality and late mortality are examined separately, the form in which each is modified, and the different causes which will determine this. Finally, an interpretation is made of the phenomena observed in Chile.

FROM THE AUTHORS' SUMMARY.

PERINATAL MORTALITY OF CHILDREN. ERICH HALFPAP, Deutsche med. Wchnschr. **79**:1172 (July 30) 1954.

While the mortality of infants during the first year of life has decreased considerably, it has been claimed that perinatal mortality (Pfaundler) did not. Perinatal mortality comprises stillborn infants, infants dying during birth, and those dying in the newborn period, which extends to the 10th day. It could be shown that in an institution considerable improvement in the perinatal mortality could be demonstrated in a period extending from 1926 to 1952.

AMBERG, Rochester, Minn.

Prematurity and Congenital Deformities

TREATMENT OF THE ANEMIA OF PREMATURE INFANTS. HANNELORE BRANDENBURG, Med. Klin. **49**:1992 (Dec. 10) 1954.

Ferro-Folsan liquidum combines ferrosulfate and folic acid. It is administered orally in amounts containing 36 to 72 mg. bivalent iron daily and 0.9 to 1.8 mg. folic acid. This medication does not prevent the first trimenon anemia of the premature infant, but when given at the age of 2 to 3 months, rapid improvement of the anemia occurs, setting in at the latest at the age of 4 months. The medication can be continued over several months.

AMBERG, Rochester, Minn.

ERYTHROBLAST AND EOSINOPHILE COUNTS OF PERIPHERAL BLOOD AS A PROGNOSTIC INDEX FOR SURVIVAL OF PREMATURE INFANTS. A. PROPERS, E. PUESCHEL, and D. WURR, Monatsschr. Kinderh. **102**:387-389 (Aug.) 1954.

Erythroblast and eosinophile counts of peripheral blood smears calculated per 100 leucocytes were performed on the 1st, 5th, and 30th days in 140 premature infants with various body weights.

It was found that infants with erythroblast counts below 15 or 16 had a favorable and those with counts above 15 or 16 an unfavorable prognosis for survival. Of 11 infants who showed high counts but did not die, erythroblast counts dropped by the fifth day of life. Infants with high initial counts who died later showed no decrease in the number of erythroblasts until death. Among the 51 infants who died only 2 had counts below 15.

Eosinophiles were present on the first day of life but dropped subsequently in all infants who died. In surviving infants eosinophile counts rose from 0 to 4 and as high as 20 within five days.

These results did not apply in premature infants with birth trauma, sepsis, syphilis, and congenital heart disease.

HARTENSTEIN, Milwaukee.

A CASE OF HEMIHYPERTROPHIA FACIEI CONGENITA. D. MOFFIE, Maandschr. Kindergeneesk. **22**:330 (Oct.) 1954.

The author describes a case of congenital hypertrophy of the right half of the face, the left half having normal proportions. On the hypertrophic side the cerebral hemisphere and the ventricles were enlarged; hydrocephalus was found caused by (partial ?) closure of the aqueduct of Sylvius.

The patient suffered from epilepsy, the electroencephalogram showing changes characteristic for continuous attacks of petit mal.

VAN CREVELD, Amsterdam.

A CASE OF CHORIO-ANGIOPAGUS PARASITICUS (ACARDIACUS) IN INEQUAL HOMOZYGOTIC TWINS. H. L. HOEKSTRA, Nederl. tijdschr. geneeesk. **98**:101-105, 1954.

A unipara was delivered of twins in the 38th week of pregnancy. X-rays during pregnancy had shown a normal and an anencephalic child. The normal child was delivered in vertex presentation, the anencephalic child in breech presentation. The cord had only a length of 14 cm. in this monster, which showed multiple defects. No lungs or heart were found. The larynx and tongue were normal. The stomach and small intestines were largely absent. There was a communication between the umbilical arterys of both children. The placentae did not differ very much. The vascular system of the monster could be considered as a branch of the circulation of the other child. The heart of the normal child showed no signs of strain, however. The circulation in the monster might have been supported to a great extent by the contractions of the capillaries in the placental villi.

VAN CREVELD, Amsterdam.

PROCONVERTIN CONTENT IN THE BLOOD OF PREMATURE INFANTS. P. VERSTEEG and E. T. B. VERSTEEGH, Nederl. tijdschr. geneesk. **98**:1296 (May 8) 1954.

The proconvertin content of the blood of premature infants is, generally spoken, much smaller than in full-term infants. The influence of the administration of vitamin K upon this content is far less pronounced than in full-term infants. This finding is thought to be related to the higher degree of unripeness of the liver in premature infants.

VAN CREVELD, Amsterdam.

Newborn

PREVENTION OF KERNICTERUS. FRED H. ALLEN JR., and LOUIS K. DIAMOND, J. A. M. A. **155**:1209 (July 31) 1954.

In utero the erythroblastotic fetus dies because he cannot make blood fast enough. After he is born he usually dies or his brain is injured because he cannot eliminate the breakdown products of his excessive blood destruction fast enough. Hence, hyperbilirubinemia is proportional to the amount of brain damage in the erythroblastotic. The exchange transfusion seems to aid the infant positively in eliminating hyperbilirubinema. Women's blood is preferred. The indications for transfusion are given: (1) clinical evidence of disease at birth with a hemoglobin of less than 15 gm.; (2) jaundice and a bilirubin of 10 mg. before the infant is 6 hours old. The aim should be to keep the bilirubin level from exceeding 20 mg. per 100 ml. Kernicterus is not

defined by the authors but seems to be used loosely to mean that brain damage that is due to the hyperbilirubinemia associated with erythroblastosis fetalis. Hence, some of the statements of the authors are not true etymologically.

KIMBALL, Evanston, Ill.

ASSAY OF THE TRYPTIC ACTIVITY OF THE FECES OF THE NEWBORN INFANT, AT TERM OR PREMATURE. FELIPE DE FILIPPE, AUGUSTO A. GIUSSANI and LEA RIVELIS, Pediatrics **14**:114 (Aug.) 1954.

The Shwachman test was carried out on 30 healthy newborn infants, including premature infants. The results were negative in 28 cases on the first day, but positive in all cases on the fourth. As it is known that normally the newborn infant, even when premature, possesses duodenal trypsin, the absence of same in the meconium indicates that it may be destroyed by intestinal stagnation. This means that the assay of fecal trypsin is of no use for the precocious diagnosis (within the four first days of life) of mucoviscidosis or cystic fibrosis of the pancreas.

FROM THE AUTHORS' SUMMARY.

AN EPIDEMIC OF DIARRHEA OF THE NEWBORN CAUSED BY ESCHERICHIA COLI O-111, B_4. CYRIL S. STULBERG, WOLF W. ZUELZER, and ANTHONY C. NOLKE, Pediatrics **14**:133 (Aug.) 1954.

An outbreak of diarrhea of the newborn in a premature nursery has been described. The result of bacteriologic, epidemiologic, and therapeutic studies identified the etiologic agent as a specific type of coliform organism, Escherichia coli O-111, B_4.

This organism was isolated in virtually pure culture from the stools of 24 premature infants who developed diarrhea. It was not found in premature infants who were effectively isolated and who remained clinically well. E. coli O-111, B_4 was not present in the stools of patients before their illness started but was isolated, again in practically pure culture, almost simultaneously with the onset of symptoms.

Neomycin proved to be an effective chemotherapeutic agent, both in eliminating the organism from the stools and causing the cessation of symptoms within a short time of each other.

Three patients died. Their case histories and postmortem findings with relation to the pathogenesis of the diseases are discussed.

FROM THE AUTHORS' SUMMARY.

PROBLEMS IN THE MANAGEMENT OF THE NEWBORN. NIVIDITA SEN, Indian J. Pediat. **21**:106-110 (May) 1954.

The author states that although problems in the management of the newborn are many, he describes one aspect only, "infection," which after birth is one of the greatest dangers to the infant.

He discusses the manner in which infections enter the respiratory and alimentary systems and the treatment that may be given. Diarrhea, thrush, eye and skin infections, infections of the meninges and the urinary tract, and congenital syphilis are all described, and the methods of treatment given.

McGUIGAN, Evanston, Ill.

ON THE TREATMENT OF THE UMBILICAL CORD IN THE NEW-BORN. PETER V. SUCKLING, South African M. J. **28**:359-361 (April 24) 1954.

Babies in a non-European maternity hospital were divided into two groups. The purpose was to prove or disprove that uncovered cords take longer to separate and to study the possible ill effects on the babies to treated.

One group was comprised of 1019 babies, whose cords were dressed daily with cord dressing and zinc and starch powder and around whom binders were secured. The other group comprised 335 babies, who were swabbed each day with methylated spirits, and no binders were secured around them.

The author feels that there is no evidence of increased risk of sepsis or hemorrhage following exposure of the umbilical cord and the avoidance of dressing and binders when daily swabbing with methylated spirits after the bath is done and that such a procedure results in a separation of the cord earlier than the usual method of dressing and binder.

McGUIGAN, Evanston, Ill.

Acute Contagious Diseases

ELECTRICAL METHODS IN DIAGNOSIS AND PROGNOSIS OF PERIPHERAL NERVE INJURIES AND POLIOMYELITIS. C. B. WYNN PARRY, Brain **76**:229 (June) 1953.

Parry reports the results of his experience with electrodiagnostic methods in cases of peripheral nerve injuries and poliomyelitis, involving 72 patients in the R. A. F. The results showed a definite pattern of electrical events in recovery from such lesions, and the use of the strength duration curves (chronaxie) and electromyography were of considerable help in the diagnosis of reinnervation and assessment of ultimate functional recovery. The earliest signs of reinnervation on the strength duration curves appeared about six weeks before the first signs of clinical recovery; on the electromyogram, about eight weeks before. In the majority of cases a diagnostic stimulator (for chronaxie studies) can afford sufficient information for all practical purposes, and the refinements of electromyography are seldom essential. However, in the differential diagnosis of lower motor neurone lesions the EMG is preeminent, for the strength duration curve is merely an assessment of the proportion of innervated to denervated muscle fibers, whereas the EMG permits the detailed examination of the individual muscle potentials themselves.

JOHNS, New York [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

ACUTE DILATATION OF THE STOMACH AS A LATE COMPLICATION OF POLIOMYELITIS. K. K. HUSSAIN, Lancet **1**:282 (Feb. 9) 1952.

Hussain reports on two patients with poliomyelitis who had spent months in respirators and then developed acute dilatation of the stomach. The first patient was a 20-year-old woman who had been in a respirator for seven months, when she developed acute dilatation of the stomach and died in five hours. There had apparently been before death a depression or paralysis of the cranial autonomic nervous system, with enlarged pupils, dry mouth, tachycardia, and the dilatation of the stomach. The gastric distention further displaced the paralyzed diaphragm and increased the pulmonary collapse, causing greater cardiac embarrassment and cerebral anoxia.

The second patient, a 25-year-old woman, had had several attacks of acute dilatation of the stomach and died three days after the last recurrence. These attacks included, in addition to the dilatation, tachycardia which did not respond to pressure on the carotid sinus, dilatation of the pupils, dryness of the mouth and dysphagia, and a poor response to carbachol and neostigmine. These findings suggest paralysis of the connector cells of the autonomic nervous system, especially in the dorsal nucleus of the vagus and the excitor cells of the parasympathetic system in Auerbach's plexus.

The author believes that the virus of poliomyelitis may cause more damage to nerve cells than is at first apparent and that certain apparently intact cells become abnormally vulnerable to oxygen lack. For this reason it is especially important to provide adequate pulmonary ventilation for respirator patients. He points out that the alkali reserve may be used as an index of adequate ventilation.

MADOW, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

FATE OF THE FACE IN POLIOMYELITIS. E. W. MOORE, Lancet **1**:1092 (May 31) 1952.

Moore reports on the degree of recovery a year or more after the onset in 14 cases of facial paralysis occurring in patients with poliomyelitis. Eight of the patients had bilateral complete paralysis of the face, and six had weakness of the lower half of the face only (partial paralysis).

When seen a year or more after the onset, all the patients with partial paralysis had completely recovered from their facial paresis without specific treatment. Recovery had taken from a few weeks up to six months, the patients with the least paralysis recovering most quickly.

Seven of the eight patients with complete paralyses still showed residual weakness, more apparent in the lower half of the face. A variable degree of recovery had taken place, mostly within the first six months. The exception was a boy of 4 years, whose complete facial paralysis had recovered completely within three months.

MADOW, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

TREATMENT OF DIPHTHERIA WITH PENICILLIN WITHOUT THE USE OF ANTITOXIN. JULIO ROMULUS CALBET and ROBERTO GONZALES HERRARA, Bol. Col. med. Habana **4**:501 (Dec.) 1953.

The authors present a large series of diphtheria patients who are treated at the Las Animas Hospital. This was divided into Group A, 520 patients who were treated solely with penicillin; Group B, 1,710 patients that were treated with antitoxin, and Group C, 237 patients that were treated with the combination of both penicillin and antitoxin. In reviewing their results they find that in Group A, there were but four deaths, or an over-all percentage of 0.76; in Group B, 120 deaths, or 7%; in Group C, 27 deaths, or 11.39%. In addition, they have noted that there were fewer myocardial and nervous complications in Group A than in either of the other two groups, and they conclude that penicillin alone is a treatment of choice in all cases of diphtheria. In fact, it has proved more efficacious than even Group C, wherein both the antitoxin and penicillin was used.

They further observed that where respiratory obstruction as a result of laryngeal diphtheria has occurred, a tracheotomy should be performed in every case. This should be followed by aerosol therapy using the Romulus cannula and frequent aspirations of the secretions. They believe that this procedure is by far more satisfactory than intubation.

PERSKY, Philadelphia [A. M. A. ARCH. OTOLARYNG.].

REMARKS OF AN EPIDEMIC OF POLIOMYELITIS. P. J. LAMBRINAKOS, D. S. MELISSAKIS, and DRIVAS HELEN PAPACOSTA, Acta pædiat. **43**:10 (Jan.) 1954.

The scientific interest roused from the study of the epidemic of poliomyelitis that broke out in the Foundlings Asylum of Athens shows that the disease caused a great morbidity; by the mere fact that 26 out of 250 infants were affected, it revealed a polymorphous clinical picture, and worthy of note is the latent form of the poliomyelitic infection of the nervous system. There is evidence to show that during the epidemic of poliomyelitis, apart from the latent forms of intestinal poliomyelitis infection reported by Mollaret, there is also a latent form of poliomyelitis infection of the nervous system, without paralysis, fever, or any other clinical manifestation, being revealed only by the well-known findings of poliomyelitis in the cerebrospinal fluid. We have been unable to find cases similar to those of third category in the available bibliography.

FROM THE AUTHORS' SUMMARY.

ACTIVE BASAL IMMUNITY AND ITS APPLICATION TO EPIDEMIOLOGY: III. COMBINED IMMUNIZATION AGAINST DIPHTHERIA, TETANUS, AND PERTUSSIS IN INFANCY. BO VAHLQUIST, LENNART HESSLEVIK, and HANS ERICSSON, Acta pædiat. **43**:15 (Jan.) 1954.

Some practical aspects of simultaneous immunization of infants against diphtheria, tetanus, and pertussis by means of mixed (triple) vaccines were investigated. Three injections were made, at 3, 4½, and 6 months of age. Mild febrile reactions occurred in 22% of the infants. Local reactions were common, particularly when a vaccine with a stronger pertussis component was employed. Three different sites of inoculation (back, arm, and leg) were compared; preference is given to the supraspinous fossa, since persistent infiltration with consequent risk of abscess was less common there. The antibody response to diphtheria and tetanus was very satisfactory. In regard to pertussis, Vaccine I (45 million pertussis bacilli per 3 cc.) gave rather low agglutinin titers, whereas Vaccine II (60 to 75 million per 3 cc.) evoked a more satisfactory response.

FROM THE AUTHORS' SUMMARY.

ACTIVE BASAL IMMUNITY AND ITS APPLICATION TO EPIDEMIOLOGY: IV. INITIAL PLAN IN DIPHTHERIA-TETANUS-PERTUSSIS VACCINATION. LENNART HESSELVIK and HANS ERICSSON, Acta pædiat. **43**:22 (Jan.) 1954.

The addition of a quick-acting local anaesthetic lidocaine (Xylocain, Astra) to aluminum-precipitated diphtheria and tetanus toxoid and to triple vaccine (diphtheria-tetanus-pertussis) was tested in human subjects. A considerable reduction of the initial pain following the injection was noted. No diminution of the immunizing effect was observed in animal experiments.

FROM THE AUTHORS' SUMMARY.

PENICILLIN TREATMENT OF SCARLET FEVER. JUSTUS STROM, Acta pædiat. **43**:32 (Jan.) 1954.

From various test series during the years 1946-1951, consisting of 6,500 cases of scarlatina, it appears that penicillin has an excellent effect in preventing complications. Not only in comparison with normally hospitalized patients, but also with entirely isolated patients, there is a clear difference in favor of treated cases. It is also shown that the peroral therapy given was, in spite of the low dosage, very little inferior to injection, from the point of view of complications. The effect in preventing complications applied particularly to the bacterial types. A difference is also apparent, however, in regard to toxic types. The only complication of this kind which proved of any significance during the years of the tests was myocarditis. According to Levander-Lindgren's investigations of the material, the frequency of myocarditis also diminished as a result of penicillin treatment. This is of particular importance in patients over 15 years of age, in whom myocarditis is of a more serious character.

FROM THE AUTHOR'S SUMMARY.

PENICILLIN IN THE PREVENTION OF SCARLET FEVER. JUSTUS STROM, Acta pædiat. **43**:38 (Jan.) 1954.

The hemolytic streptococci are extremely sensitive to penicillin, as a rule requiring a concentration of only 0.03 I.U. per milliliter serum. It is possible to obtain a rapid effect in respect to sanitization of the nose and throat by administration of penicillin by injection or perorally. Recurrences in hospitals, as also secondary cases among staffs, have thereby been practically eliminated.

The streptococci reappeared, however, in an extensive number of cases a week after the return home, to the extent of 6.4% of patients treated by injection and 14.2% of those treated perorally. The so-called return cases have nevertheless been rare. Their number has been reduced by penicillin therapy to between 1/20 and 1/40 of the earlier frequency, or about 1 to 2 per 1,000. Peroral therapy has proved almost as effective as injection treatment for the prevention of return cases in spite of a far greater frequency in the recurrence of streptococci.

Sanitization of the environment from which the scarlatina patient comes is of great importance in combating diseases caused by hemolytic streptococci, as also for the prevention of recrudescence after the return home. Such sanitization measures should be adopted after every case of scarlatina, and should be carried out in stages.

FROM THE AUTHOR'S SUMMARY.

Acute Infectious Diseases

REVIEW OF RHEUMATIC DISEASES. HANS WAINE, A. M. A. Arch. Int. Med. **93**:121 (Jan.) 1954.

The author has reviewed all of the important literature published in 1951 and 1952 pertaining to rheumatic diseases. He discusses the work which has been done on preventative measures and treatment of rheumatic fever, and he summarizes the work which has been done by the American Heart Association and the Empire Research Council in regard to the comparative values of cortisone, corticotropin, and salicylate. Preliminary analysis indicates that the individual manifestations of rheumatic fever have abated to equal degree following the use of any one of the three drugs. No conclusions can be drawn at present as to the superiority of any one of these agents. It is recommended that the steroids be used in the acutely ill patients. This article provides an extensive bibliography on this subject covering the indicated time period.

JONES, Chicago.

CARRIERS OF HEPATITIS VIRUS IN THE BLOOD AND VIRAL HEPATITIS IN WHOLE BLOOD RECIPIENTS. JOHN R. NEEFE, ROBERT F. NORRIS, JOHN G. REINHOLD, CHARLES B. MITCHELL, and DAVID S. HOWELL, J. A. M. A. **154**:1066 (March 27) 1954.

The development of hepatitis in several blood recipients from three blood donors who are carriers of hepatitis virus B is described. None of these donors had ever been jaundiced, but two had abnormal liver function tests. One, however, was absolutely "silent." From accumulated data it is estimated that from 0.2% to 0.5% of the population carry hepatitis virus B in their blood streams. Easy methods of detection and eradication of the virus in whole blood are needed.

KIMBALL, Evanston, Ill.

INFECTION WITH THE VIRUS OF HERPES SIMPLEX. T. F. MCNAIR SCOTT, New England J. Med. **250**:183 (Feb. 4) 1954.

When illness due to the virus of herpes simplex develops, there are usually two components. The first is a local vesicular eruption on the skin or mucous membranes. The second may be a generalized, systemic invasion that is often severe and occasionally fatal.

After recovery the patient carries the virus in a latent state, and circulating antibodies are present in the blood. The latent virus may produce recurrent "fever blisters" if the host's physiologic environment is altered by injury, disease, or some occult intrinsic change. The circulating antibodies usually prevent a systemic invasion.

The diseases that may be caused by a first exposure to the herpes simplex are classified as follows:

Skin
- Herpes simplex
- Eczema herpeticum
- Traumatic herpes

Mucous membranes
- Acute gingivostomatitis
- Recurrent stomatitis?

Central nervous system
- Meningoencephalitis

Mucocutaneous junction
- Herpes labialis
- Herpes progenitalis
- Vulvovaginitis

Eye
- Conjunctivitis
- Keratoconjunctivitis

Generalized infection
- Hepatitis of newborn

The authors differentiate herpangina from herpetic gingivostomatitis by the localization of the lesions of the former to the posterior part of the mouth, and by the presence of other cases of herpangina in the community.

A differentiation between "eczema vaccinatum" and "eczema herpeticum" can be made by the presence of lesions all at the same stage of development in the former and lesions of different stages of development in the latter.

The diagnosis of diseases caused by the herpes virus can be made in four ways: virus isolation, serologic tests, histologic examinations of fluid or tissues, and electron microscopy.

Suggestions for treatment are given for both adult and children's infections, and there is a discussion of the epidemiology of herpes infections. WHEELOCK, Denver.

RHEUMATIC FEVER PROPHYLAXIS. ROBERT A. TIDWELL, Northwest Med. **53**:470 (May) 1954.

The author reports the use of a single daily dose of a slowly excreted penicillin (Bicillin) in the prophylaxis of recurrent attacks of rheumatic fever. The series consisted of 59 patients, 25 of whom were ill at the beginning of the program.

The single dose of penicillin was highly effective in eradicating the Streptococcus from the oropharynx. There was no recurrence of rheumatic fever in any of the patients treated, and school absenteeism was reduced 80.4% over a control period. DOCTOR, Seattle.

Chronic Infectious Diseases

TREATMENT OF TUBERCULOUS MENINGITIS. ANTONIO PACI, Riv. clin. pediat. **51**:1 (Jan.) 1953.

The author reports on 69 cases of tuberculous meningitis observed in the Department of Pediatrics of the University of Pisa from 1947 to 1952. Results of treatment and the obstacles that can be encountered are stated. Treatment cannot be standardized but needs special attention and care in each case.

As the technique of treatment improved, the results were also better. There have been 25 cases completely cured that have remained cured. In some cases, postmortem effects were observed.

The author confirms the absolute necessity of early treatment, prolonged and continuous, with careful and vigilant control of each individual case. FROM THE AUTHOR'S SUMMARY.

TOXOPLASMOSIS. BERNARDO PEREZ MORENA, Acta pediat. españ. **11**:375 (June) 1953.

This is a brief study of the history of the discovery of toxoplasmosis, the modes of transmission, the pathology of the disease, and methods of diagnosis and treatment. The treatment is not satisfactory, but the author feels that the treatment suggested by Gaetano Boschi is of some value in the meningoencephalitic form of the disease. Chlortetracycline (Aureomycin) and oxytetracycline (Terramycin) may be of value.

ALLEN, Santa Fe, N. Mex.

A STUDY OF THE PHENOMENON OF RELAPSE IN CASES OF TUBERCULOUS MENINGITIS TREATED BY STREPTOMYCIN. ROBERT DUBOIS and POL GILLET, Rev. españ. pediat. **9**:799 (Sept.-Oct.) 1953.

The authors report on the results in the treatment of 302 cases of tuberculous meningitis treated at the pediatric clinic of the University of Brussels.

These cases include those dating from 1946 to the present. Relapses are much more common in cases prior to 1949, when smaller dosage with a shorter period of treatment was the rule. After 1949, the incidence of relapses is much less. The details regarding the alterations in the spinal fluid lead the authors to believe that it is imperative that the spinal fluid be clear before treatment is discontinued. Some of the relapses were very early and others suffered exacerbation after a year or two, but all relapses were in the group which had minimal therapy. The authors do not believe that the cases with recurrent bouts had been cured and then developed a new case, but that they had not acquired adequate immunity because of the short-term therapy.

ALLEN, Santa Fe, N. Mex.

PHARYNGEAL AND BRONCHIAL TUBERCULOSIS IN INFANCY: A COMPARATIVE STUDY OF THE USE OF HYDRAZIDE OF ISONICOTINIC ACID, STREPTOMYCIN, PAS AND TBI. R. POCH VINALS, M. IRIONDO SEGURA, and J. L. CONCELLON, Acta oto-rino-laring. ibero-am. **5**:260, 1954.

The authors present a series of nine cases of pharyngeal and tracheobronchial tuberculosis in children ranging in age from 7 months to 9 years. These patients were given the various antibiotics, including streptomycin, paraaminosalicylic acid (PAS), the hydrazide of isonicotinic acid, and a thiosemicarbazone preparation (TBI). In the experience of the authors the hydrazide of isonicotinic acid appears to be the most efficacious drug. Their recommendation is that the minimal dose of this drug should be from 20 to 25 mg. per kilogram of body weight. This new drug seems to prevent caseous destruction of the lymph nodes if given early. They also believe that bronchoscopic treatment should be supplemented to the routine treatment instituted. This often would prevent atelectasis and rupture of the caseous gland into the lung. The authors did not have a single case of frank stenosis of the bronchi, and they also believe that with this new medication there is much less of a chance for cicatricial stenosis.

PERSKY, Philadelphia [A. M. A. ARCH. OTOLARYNG.].

SECONDARY SUPPURATIVE GLANDS AFTER INTRADERMAL VACCINATION WITH BCG: TREATMENT WITH ISONIAZID. MARION GONZALES and OSVALDO MONTES, Rev. chilena pediat. **25**:86 (Feb.) 1954.

Isoniazid is a highly effective drug for suppurating adenitis secondary to BCG vaccination. The basis of treatment consists in the local use of the drug in doses of 2 to 30 mg. per injection. Its common use is reduced to some rebellious fistulized cases, and the necessary daily dose is 5 mg. per kilogram of body weight.

FROM THE AUTHORS' SUMMARY.

CASE OF INTRAUTERINE TUBERCULOSIS. JULIO ESPINOZA, HUMBERTO RECCHIONE, and GUILLERMO GARCIA, Rev. chilena pediat. **25**:88 (Feb.) 1954.

The authors publish the case history of a premature son of a tuberculous mother with whom he lived four hours. The infant died 26 days later; the autopsy showed a disseminated tuberculosis of an exudative caseous type, predominantly pulmonary, which is cataloged as of intrauterine origin. The pathogenesis of this rare form of tuberculosis is commented on.

FROM THE AUTHORS' SUMMARY.

THE INFLUENCE OF VARICELLA AND MEASLES ON THE COURSE OF TREATMENT OF TUBERCULOUS MENINGITIS. MAZUDE GUSTIN KAIRUZ and JORGE E. HOWARD, Rev. chilena pediat. **25**:124 (June) 1954.

The influence that chicken pox or measles might have on the course of tuberculous meningitis is analyzed.

Of 171 patients studied, 23 had chicken pox as the intercurrent sickness and 8 had measles. As a control group, an equal number of cases of tuberculous meningitis without these diseases were taken from the general files. In each patient the general development of the disease was studied, as well as the fever chart belonging to the intercurrent illness, the variations of the different elements of the cerebrospinal fluid, and the sedimentation rate in serial examinations.

The results indicate no unfavourable action of these intercurrent infections on the course of tuberculous meningitis. The authors assign great importance to these findings, as they permit them not to modify either treatment or prognosis.

FROM THE AUTHORS' SUMMARY.

DEVELOPMENT, SIGNIFICANCE, SEQUELAE, AND TREATMENT OF LYMPH NODE RUPTURE IN CHILDREN WITH TUBERCULOSIS. OTTO BOSSERT and WILLI PLETTENBERG, Deutsche med. Wchnschr. **79**:665 (April 23) 1954.

The authors discuss the rupture of tuberculous lymph nodes into a bronchus, citing six illustrative cases whose ages varied from 8 months to 11 years, occurring under treatment with streptomycin and isoniazid. In presence of uncomplicated hilus processes, treatment with antibiotics and chemotherapeutic agents should not be begun immediately in infancy.

AMBERG, Rochester, Minn.

PROTECTION OF CHILDREN FROM TUBERCULOSIS BY BCG VACCINATION. MARIA DAELEN and ELISABETH DIX, Monatsschr. Kinderh. **101**:517 (Dec.) 1953.

During a four-year period of observation 45 children among 70,424 vaccinated with BCG, ranging in ages from 3 to 18 years, developed tuberculosis. During the same period, 318 developed tuberculosis among the nonvaccinated control group of 92,145 children. With corrected figures this corresponds to a morbidity of 0.6 per 1,000 children for the BCG group and 3.5 for the control, a ratio of 1 : 5.7.

Despite more contact with tuberculosis, the morbidity of BCG-vaccinated urban children was not higher than that of the rural group, whereas urban children in the control series had a higher incidence than the rural control children.

There was only a very small occurrence of conversion to tuberculin-negative among children who had received BCG. BCG vaccination is advocated, especially for urban children.

HARTENSTEIN, Syracuse, N. Y.

PERSISTENCE OF TUBERCULIN SENSITIVITY IN BCG VACCINATED PERSONS ISOLATED IN INSTITUTIONS. OLE WASZ-HOCKERT and MARTA DONNER, Acta pædiat. **43**:103 (March) 1954.

A preliminary report is given on investigations into the duration of sensitivity to tuberculin of 217 BCG-vaccinated inmates of closed institutions. Both the inmates and the staff were under strict observation for tuberculosis. The results obtained are as follows: 1. The isolated milieu has been effective in excluding the risk of tuberculous infection. No increased allergy suggestive of super-infection was observed. 2. The patients examined were vaccinated with BCG vaccine from the bacteriological laboratory of Sahlgrenska Sjukhuset, Gothenburg; 0.1 ml. containing 0.05 mg. of BCG organisms was injected intracutaneously into the left thigh. Of those vaccinated, 96.4% were positive at the check-up. 3. The tuberculin reaction has been taken as negative if smaller than 10 by 10 mm. 72 hours after the injection of 1.0 mg. of dilute old tuberculin (Mantoux). 4. Two cases in which Koch's phenomenon was observed were excluded from the material. 5. After one year, 7.3% had become negative; after two years, 16.0%; after two and one-half years, 28.3%, and after three and one-half years, 29.4%. 6. Mantoux test 0.01, 0.1, and 1.0 mg. on the vaccinated showed that allergy to tuberculin, on the whole, declined with time, which supports the above result.

FROM THE AUTHORS' SUMMARY.

SELECTIVE FILTRATION OF SYPHILITIC REAGINS THROUGH THE PLACENTA. ELSE VOGT, Acta pædiat. **43**:247 (May) 1954.

Selective filtration of syphilitic reagins through the placenta is studied. Three serologic tests for syphilis performed on the serum from 107 newborn infants are compared with the same tests on the serum from their mothers prior to delivery. Meinicke's clarification reaction (MKR) was negative in the serum from all 107 infants, even where the serum reagin titer of the mother was high at the time of delivery, and the other tests were positive in the serum of the infant. It is concluded that MKR is not suitable for the detection of syphilitic reagins in the serum from newborn infants because the reaction is always negative.

FROM THE AUTHOR'S SUMMARY.

ON TUBERCULOSIS OF THE BONE AND JOINT OF BCG VACCINATED CHILDREN. ALF BACKMAN and ERIC IVAR WALLGREN, Acta pædiat. **43**:252 (May) 1954.

No harmful effect of BCG vaccination has been found in the present group of 17 cases of bone and joint tuberculosis occurring in adequately vaccinated subjects. In these cases the disease has taken a mild course; however, the number is too small to permit of any definite conclusions. In only two of the cases a strong exposure had occurred, in the others only a slight one, or exposure was not detected.

FROM THE AUTHORS' SUMMARY.

THE EFFECT OF HYALURONIDASE ON THE MORO EPIDERMAL TUBERCULIN REACTION. C. CHOREMIA, C. PAEDIATELIS, A. GAZOULIS, and D. ZOUMBOULAKIS, Acta pædiat. **43**:264 (May) 1954.

Admixture of hyaluronidase of old tuberculin and purified protein derivative (PPD) for percutaneous tests produced a stronger and more rapid reaction in tuberculin-positive children.

FROM THE AUTHORS' SUMMARY.

Diseases of Blood, Heart and Blood Vessels, and Spleen

VENTRICULAR SEPTAL DEFECT IN INFANCY. MARY ALLEN ENGLE, Pediatrics **14**:16 (July) 1954.

The clinical features and postmortem findings have been analyzed in nine infants who had a ventricular septal defect and died in heart failure. Possible explanations for the severity of the manifestations of this simple and common defect were considered. The differential diagnosis from other conditions associated during infancy with cardiac enlargement and pulmonary congestion was discussed. It is hoped that an awareness of the serious consequences of this malformation in certain patients and the ability to diagnose it accurately will be forerunners of successful surgery to correct the defect.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL ABSENCE OF A PULMONARY ARTERY: ITS DEMONSTRATION BY ROENTGENOGRAPHY. STANLEY M. WYMAN, Radiology **62**:321, 1954.

Three cases, aged 15, 6, and 20 years, with congenital absence of a pulmonary artery are added to the literature. The defect was left-sided in two and right-sided in one. All were demonstrated on conventional films and by angiocardiography: In each case a network of small vessels was apparent and formed a lace-like pattern in striking contrast to the broad branching vessels usually seen. The involved hemithorax appeared to be reduced in size. The rib interspaces were smaller, the diaphragm elevated, and mediastinal structures displaced toward the affected side. The pulmonary artery shadow was absent even in overexposed films. In two cases, there was herniation of the normal lung anteriorly toward the affected side. In all there was no evidence of a shift of the mediastinum or heart with inspiration .

The author concludes that the absence of a pulmonary artery and the coexistence of enlarged bronchial arteries can be recognized on roentgenograms of the proper penetration, but the true nature of the condition can best be established by angiocardiography. Anspach, Chicago.

CORRELATION OF UPPER LOBE VASCULARIZATION WITH CERTAIN CONGENITAL INTRACARDIAC SHUNTS. N. G. DEMBY and A. P. GEWANTER, Radiology **62**:329 1954.

In the authors' experience, abnormal intracardiac shunts have been a frequent cause of alarming dyspnea and cyanosis, even though the size and contour of the heart early in life may be normal. This often has led to an erroneous diagnosis of atelectasis or aspiration pneumonitis. The clouding in the lung really represented an anomalous blood flow which was overlooked or misinterrupted. Serial films, paying special attention to the size of peripheral vessels, aided in predicting the type of anomaly.

The authors conclude that early right upper lobe infiltration with abnormal cardiac size and shape on roentgenogram would suggest transposition of the great vessels as a first possibility and interventricular septal defects as a second, with a common denominator of a large pulmonary artery. Both carry a fatal prognosis. Eight cases are described in detail.

Anspach, Chicago.

CONGENITAL AND FAMILIAL AFIBRINOGENEMIA, WITH SPECIAL REFERENCE TO THREE PERSONAL CASES. L. CAUSSADE, N. NEIMANN, M. PIERSON, and M. MANCIAUX, Presse méd. Supp. 49, p. 1040, July 7, 1954.

Congenital and familial afibrinogenemia is a very uncommon condition, holding a quite special place among the pseudohemophilic diatheses of the young.

The authors could collect only 19 cases from the world literature and are today reporting 3 personal cases concerning 3 sisters, respectively aged 8½ years, 2 years, and a few weeks. A fourth sister died at 2 days of age from an umbilical hemorrhage. The parents, in good health though affected by hypofibrinemia, were first cousins. Through these 22 analyzed case histories, this very rare condition is studied by the authors.

Clinically, afibrinemia is manifested by early, severe, induced hemorrhages, superficial ecchymoses, and hematomas with a serious prognosis.

Hematologically, blood platelets, capillary resistance, and bleeding time are usually normal, but the clotting-time is unlimited and the sedimentation rate markedly slackened. Almost total absence of fibrinogen—therefore of fibrin—in the circulating blood is evidenced by various chemical, immunological, and electrophoretic methods.

The genetic problem remains obscure. Although the part of heredity, consanguinity, and familial incidence is well established, one is reduced to hypotheses as regards the intrinsic nature of the defect and its mode of transmission.

The therapy is a supplementive one, with supply of blood, plasma, and above all, extractive fibrinogen; but the rapid clearance of the injected fibrinogen implies a greater difficulty in the treatment. The authors emphasize the possible relationship of this diathesis to neighoring syndromes, such as major constitutional hypofibrinemia and minor latent hypofibrinemia.

FROM THE AUTHORS' SUMMARY.

HEMOLYSIS AND ACQUIRED HEMOLYTIC DISEASES. C. GASSER, Helvet. paediat. acta **9**:135 (June) 1954.

The inherent and foreign influence on erythrocytes is presented in the first general part. Thereafter the theoretical basis of diagnostic possibilities is discussed by proving in vivo and vitro the clinical symptoms of hematological charges and therapy. In a second special part the hemolytic anemias are separated into the corpuscular (erythrocytic) and extracorpuscular (plasmatic) forms. To the extracorpuscular forms belong all the anemias caused by toxins and immune antibodies. Under the toxic hematologic anemias those caused by medications and those by infection are treated at greater length. From the large group of hemolytic anemias caused by antibodies are treated next the various forms and genesis of hemolytic diseases of the newborn; then the hemolytic reactions caused by transfusions, and finally the heterogenous group of acquired hemolytic anemias of unknown origin which have the appearance of unspecific blood group auto- and isoantibodies. In conclusion it is shown here that acquired erythrocytic defects as seen in various deficiency anemias may also lead to a certain degree of hemolysis.

FROM THE AUTHOR'S SUMMARY.

THE ACTION OF HYALURONIDASE ON HEMOGENIC TESTS. O. LANCIANO and L. PALMARDITA, Arch. ital. pediat. e puericolt. **16**:406, 1954.

The action of hyaluronidase on coagulation time (10 cases), clot retraction (20 cases), prothrombin time (10 cases), and platelet agglutination (10 cases) is investigated. In opposition to what was observed by other authors, hyaluronidase has no influence on the clotting time when a pure preparation is used that is without the addition of sodium chloride as is generally the case in commercial preparations. Some variations were found, instead, in the clot contraction (after McFarlane's technique) mostly in the sense of a more marked phenomenon. As other authors have already observed, the prothrombin time remained unvaried after the addition of the enzyme, while the platelet agglutination, held as absent in other researches, showed slight variations when hyaluronidase was present.

FROM THE AUTHORS' SUMMARY.

Diseases of Nose, Throat, and Ear

LYMPHOSARCOMA OF THE TONSIL IN CHILDREN. BATES F. METSON, Ann. Otol. Rhin. & Laryng. **63**:193 (March) 1954.

Metson reviews the literature on lymphosarcoma of the tonsil in children, finding six cases. All the reported patients were male children, and all died within a few weeks to four months after the diagnosis of lymphosarcoma was made. The author reports a case of his own occurring in a girl 2½ years of age.

The histopathologic diagnosis of lymphosarcoma of the tonsil presents difficult differentiation from highly anaplastic squamous-cell carcinoma. Also, it is difficult to classify the lesion as to type of sarcoma from tissue study alone.

Clinically, when unilateral tonsillar enlargement or marked asymmetry of the tonsils is encountered, one should give ample consideration to malignancy in the differential diagnosis. The suspicion of malignancy should not be discarded after one negative biopsy, as this is a fairly common misleading occurrence in lymphosarcoma of the tonsil.

The treatment of the author's patient was the same as that given in most of the cases previously reported, namely, tonsillectomy followed by roentgen therapy. The outcome was fatal in spite of response of the local pathologic lesion to treatment. This was likewise true in the reported cases.

STEELE, Kansas City, Kan. [A. M. A. ARCH. OTOLARYNG.].

PEDIATRIC ASPECTS OF THE TONSIL PROBLEM. A. TOW, Eye, Ear, Nose & Throat Month. **33**:33 (Jan.) 1954.

Tonsillectomy and adenoidectomy should be performed only when there is a positive indication for the procedure. If the tonsils or adenoids are hypertrophied to the degree where they mechanically interfere either with deglutition or with respiration, they should be removed. Recurrent infection associated with the tonsils or adenoids is another positive indication for operation. This is especially true in a puny child who has failed to gain normally in weight. In those diseases in which the tonsils are condemned as a focus of infection, it is best to make a decision as to operation based on the appearance of the tonsils and on the history related to tonsillar infection. The decision in each case must be individualized. Tow believes that the removal of adenoids alone is justified in only the rare case. Tonsil and adenoid operations should not be performed during the months when poliomyelitis is prevalent. Although the incidence of poliomyelitis may not be greater in children who have had a tonsillectomy within two months of the disease, the bulbar form develops almost twice as frequently.

JENNES, Waterbury, Conn. [A. M. A. ARCH. OTOLARYNG.].

THE TONSIL PROBLEM IN THE ALLERGIC CHILD. L. S. NELSON and A. V. STOESSER, Eye, Ear, Nose & Throat Month. **33**:34 (Jan.) 1954.

In a discussion of this controversial problem, Nelson and Stoesser conclude that tonsillectomy should be performed in allergic patients only when positive indications exist for tonsil removal. If the tonsils are removed because of local disease of the tonsil and not in an effort to improve the allergy, the procedure will be beneficial to the allergic child. It should be performed only after the undelying allergic process has been completely investigated and adequate treatment has been instituted. The operated-on child must be maintained in good allergic control because of the increased tendency for regrowth of lymphoid tissue in the presence of uncontrolled allergy.

JENNES, Waterbury, Conn. [A. M. A. ARCH. OTOLARYNG.].

CHOICE OF ANESTHESIA FOR TONSILLECTOMY. S. H. AXELROD, Eye, Ear, Nose & Throat Month. **33**:36 (Jan.) 1954.

Basal anesthesia should be utilized for children, both for psychic reasons and as a prelude to smooth uneventful anesthesia. Axelrod prefers paraldehyde administered in combination with olive oil and benzyl alcohol as a retention enema. Vinyl ether is used for induction, after which the patient is intubated orally under open-drop ether. The advantages of endotracheal intubation outweigh its disadvantages. The tube should be of correct size; inflatable cuffs should not be employed in children, and the tube should be sterilized adequately before use. With a meticulous atraumatic technique during the proper plane of anesthesia, endotracheal anesthesia in children provides a safer anesthesia and is without untoward effects to the delicate tissues of the larynx.

Local anesthesia is the method of choice for adults. Careful injection of the anesthetic agent is necessary in order to obtain a good anesthesia. Axelrod favors nerve-block anesthesia, with accurate anatomic instillation of the anesthetic agent. For those adults who reject a local anesthesia for tonsillectomy, general anesthesia with the endotracheal technique is a necessity.

JENNES, Waterbury, Conn. [A. M. A. ARCH. OTOLARYNG.].

THE TONSIL PROBLEM IN REVIEW. A. R. HOLLENDER, Eye, Ear, Nose & Throat Month. **33**:44 (Jan.) 1954.

Discussion of the functions of the tonsil must be limited to theoretic reasoning in the absence of factual knowledge on this subject. It is believed that there is a relationship between the tonsil and the ability to acquire immunity. In the medical treatment of tonsillitis, the new trends in therapy with utilization of antibacterial agents have substantially improved the prognosis of the disease. More frequent use of the laboratory for supportive diagnosis of the type of tonsillitis will be helpful in determining the correct therapy. The treatment of chronic tonsillitis is a problem in management, because it is difficult at times to decide whether a conservative or radical attitude should be adopted. There is no disagreement as to the value of tonsillectomy once the indications are absolute. Often tonsillectomy has been indicated as a failure on the basis of technical grounds. The author quotes Boies: "When a tonsil operation is performed by one adequately trained, and with good technique, it is a highly satisfactory procedure in terms of the end results. . . ." In selected cases which are unsuitable for tonsillectomy, roentgen-ray therapy has proved very useful.

JENNES, Waterbury, Conn. [A. M. A. ARCH. OTOLARYNG.].

TREATMENT OF OTITIS MEDIA AND EXTERNA WITH A NEW ANTIBIOTIC COMBINATION. A. M. LAZAR and M. GOLDIN, Eye, Ear, Nose & Throat Month. **33**:351 (June) 1954.

Proper treatment of infections of the external and middle ears depends upon adequate consideration of the bacteriology. It is important to consider each case individually with appropriate bacteriologic studies and with determination of the sensitivity of the infecting bacteria to various antibiotic or chemotherapeutic agents. Fungi constitute a minor cause of external otitis. Staphylococci or other Gram-positive organisms invariably cause circumscribed otitis externa, whereas Pseudomonas aeruginosa, Proteus vulgaris and other Gram-negative bacteria are the causative organisms in the diffuse type of otitis externa. Otitis media was formerly considered to be primarily due to Gram-positive bacteria, but studies in recent years indicate that Gram-negative organisms are becoming increasingly more important in this regard. This may be partly due to the increasingly widespread usage of antibiotics which are effective against Gram-positive bacteria, which are then replaced by Gram-negative bacteria.

Because of the wide variety of organisms responsible for ear infections and the marked differences in the sensitivities of these organisms to different therapeutic agents, the ideal medication for treatment of infections of the ear is one that is effective against the widest range of organisms. Lazar and Goldin report on the use of a new drug, Biomydrin Otic, which incorporates neomycin, gramicidin, Thonzonium Bromide, and thonzylamine hydrochloride in an aqueous, isotonic solution buffered at pH 6.2. Neomycin is effective against a very wide spectrum of both Gram-positive and Gram-negative organisms and is particularly effective against infections due to P. aeruginosa and staphylococci. Both gramicidin and Thonzonium Bromide are effective against Gram-positive organisms. Thonzylamine hydrochloride exhibits local anesthetic and antipruritic properties. Thonzonium Bromide is also an effective mucolytic agent and a powerful wetting agent.

A total of 282 patients were studied, including 150 children and 132 adults. These cases included four groups: suppurative otitis media, nonsuppurative otitis media, circumscribed otitis externa, and diffuse otitis externa. Treatment was considered to be successful in 88.7%, with only 11.3% considered as failing to respond to treatment. However, successful treatment included both complete cures and moderate to marked improvement. Of the 250 patients classified as successful, only 112, or 45%, obtained complete cures.

Treatment of external otitis consisted in careful cleansing of the canal followed by 4 drops of the drug instilled into the ear three times daily. Treatment of suppurative otitis media consisted in 4 drops of the medication instilled into the ear three times daily, with the flow of the drug facilitated by gentle pressure on the tragus. Usually no other therapy was employed. The superior effectiveness of this ear medication is attributed to its component drugs and to the aqueous vehicle properly adjusted to the correct, slightly acid reaction.

JENNES, Waterbury, Conn. [A. M. A. ARCH. OTOLARYNG.].

SOME TONSIL PROBLEMS. C. J. HEINBERG, Eye, Ear, Nose & Throat Month. **33**:470 (Aug.) 1954.

Tonsillectomy-adenoidectomy should not be considered as a minor procedure because of the possible hazards involved. In young children there is also the risk of undesirable personality changes subsequent to hospitalization and the operation. It is helpful to describe to the child the hospital environment and the anesthetic at the office prior to hospitalization. Heinberg prefers vinyl ether induction, followed by ether vapor, for children, with maintenance in the second plane of anesthesia. The patient does not leave the operating-room table until all reflexes have completely returned. In adults preoperative sedation of morphine and atropine is used, and for local anesthesia Heinberg uses 2% procaine hydrochloride (Novocain) with hyaluronidase and epinephrine. For general anesthesia he prefers induction with cyclopropane with a change over to ether or, in some cases, a very light thiopental (Pentothal) sodium anesthesia combined with local procaine hydrochloride. All operations are performed with patients in the supine position. Immediate hemorrhage is controlled by clamping and tying all bleeding vessels. A combination of rutin and ascorbic acid is used in order to decrease the incidence and amount of bleeding, both immediate and late. Heinberg is of the opinion that tonsillectomy and adenoidectomy can be safely performed during the so-called "polio season" except in the presence of an active epidemic.

JENNES, Waterbury, Conn. [A. M. A. ARCH. OTOLARYNG.].

TECHNIQUE OF REMOVAL OF ADENOID TISSUE OF THE NASOPHARYNX IN CHILDREN. PHILIP E. MELTZER, J. A. M. A. **154**:228 (Jan. 16) 1954.

A technique for removing adenoid tissue under direct vision is described. This method enables the operator to get all the tissue surrounding the eustachian tubes and thus prevent recurring hearing loss from tubal closure.

KIMBALL, Evanston, Ill.

THE INARTICULATE CHILD: A PROBLEM IN DIAGNOSIS. J. W. MCLAURIN, Laryngoscope **64**:454 (June) 1954.

There are several reasons, in addition to deafness, why a child may be inarticulate. He may be aphasic because of brain damage, he may have a psychic block, or there may be a functional cause. A great responsibility rests upon the physician to recognize the condition, for early treatment is most important.

The intricate tests, such as psychogalvanic skin resistance, audiometry, electroencephalography, and pure-tone audiometry by peep-show methods, are difficult to perform, require elaborate apparatus and special training to operate, and cannot well be used on very young children.

McLaurin considers it unfortunate that the impression that such methods are necessary for diagnosis is so prevalent. The otologist should know the detailed speech and hearing and other developmental stages of the normal child. These stages are explained. If there is no speech (single words) at 12 months or no response to sound at 16 months, there probably is an abnormality.

To diagnose a child's hearing loss there must be a very complete history, the details of which are given. The child is observed carefully, making every effort to put the child at ease. Calibrated noise makers are generally used while the child plays. The cessation of a child's activity is used

as the indication of the child's being conscious of the sound. There must be observation of the child's facial expression, use of gestures, motor behavior, social perception, and other characteristics. These not only help to evaluate the hearing loss but also to differentiate it from other lesions.

HITSCHLER, Philadelphia [A. M. A. ARCH. OTOLARYNG.].

A REVIEW OF 1,000 CONSECUTIVE CLOSED FOSSA TONSILLECTOMIES WITHOUT SPONTANEOUS HEMORRHAGE. ERNEST B. EMERSON JR., New York J. Med. **54**:2339 (Aug. 15) 1954.

Emerson, from the University of Rochester School of Medicine and Dentistry, describes his technique for preventing late hemorrhage after tonsil removal. He says that there has been a general refusal of tonsil surgeons to recognize that bleeding is due to "a hole in a blood vessel not enclosed in a suture." He ridicules such "causes" as spring of the year, menstruation, temperature, etc. This is his second report; the first covered 624 cases published in the *Journal of the American Medical Association*, May 24, 1952. He uses blunt dissection and avoids the tonsillotome because of "tags left behind." Sutures are placed in the tonsil bed and are so set as to take in muscle but to avoid the pillars. Since the blood vessels follow the axis "from pole to pole," all sutures, theoretically at least, surround the vessels and ligate them. Thus the fossa is narrowed or "closed," according to Emerson's terminology. A perfect score was obtained in these 1,000 cases.

ABSTRACTOR'S COMMENT: Bleeding arteries during tonsil surgery have been clamped and tied by all good operators for many years, yet in some cases a slough may open a blood vessel as late as the 13th day (personal experience). Moreover, there are instances of diffuse capillary or small artery bleeding in which styptics and compression are necessary. Also, certain blood dyscrasias, e. g., hemophilia, are responsible for poor clotting and healing time. As for "tags," they occur under any technique, and must be removed. In these days no tonsillectomist will allow a patient to leave the operating room until all bleeding has stopped.

I. W. VOORHEES, New York [A. M. A. ARCH. OTOLARYNG.].

THE PERACUTE MALIGNANT LARYNGOTRACHEOBRONCHITIS OF YOUNG CHILDREN. F. ESCHER, Schweiz. med. Wchnschr. **84**:67 (Jan. 9) 1954.

This paper is a discussion of the results of the treatment of acute malignant laryngotracheobronchitis in 24 cases. Two of these died before treatment could be instituted. In 22 cases, tracheotomy was combined with bronchoscopy, so that 18 of the patients could be saved. Additional treatment is discussed.

AMBERG, Rochester, Minn.

THE DEMONSTRATION OF INFLUENZA VIRUS IN CASES OF PERACUTE LARYNGOTRACHEOBRONCHITIS OF YOUNG CHILDREN. F. ESCHER and H. LOFFLER, Schweiz. med. Wchnschr. **84**:920 (Aug. 7) 1954.

From material obtained directly from the trachea in two cases of paracute laryngotracheobronchitis maligna, one of which recovered, influenza virus A′ could be isolated. In the third case, where this organism could not be isolated, the serologic test was positive.

AMBERG, Rochester, Minn.

DEAFNESS AND DEAF-MUTISM IN CHILDREN, WITH SPECIAL REFERENCE TO RUBELLA. BERTEL IVSTAM, Nord. med. **49**:208 (Feb. 6) 1953.

The author reports on a study of 496 children born from 1935 to 1942 and attending Swedish schools for deaf-mutes. The study was performed in 1951. Congenital deaf-mutism was due to heredity in 150 cases, to antenatal rubella in 31 cases, and to an unknown genesis in 238 cases. In 77 cases there was a postnatal acquired deaf-mutism due to birth trauma, erythroblastosis, meningitis, and different kinds of infections. The author maintains that there exists an association between the incidence of maternal infection with rubella during the early months of pregnancy and the incidence of congenital deaf-mutism. Out of the 29 children of mothers who had had rubella during the first four months of pregnancy, only 1 was found to have congenital defects (organic heart disease and dental malformation). The risk of congenital anomalies in infants of mothers infected with rubella during the first few months of pregnancy is therefore small and does not justify abortion.

WALLGREN, Stockholm.

ACUTE STENOSING LARYNGOTRACHEOBRONCHITIS. J. FALBE-HANSEN, Nord. med. **50**:1091 (Aug. 6) 1953.

The author reports on 24 cases of acute stenosing laryngotracheobronchitis in children 2 months to 7 years of age (18 boys, 6 girls). Tracheotomy was performed in all cases. Sometimes the laryngitis was subglottic without a descending infection, sometimes supraglottic without or with a descending infection. The worst prognosis was in the subglottic laryngitis with descending infection. The mortality rate was 37%. Early tracheotomy performed under general anesthesia after intubation and tracheobronchial suction is recommended.

WALLGREN, Stockholm.

A BACTERIOLOGICAL STUDY OF ACUTE LARYNGITIS IN CHILDREN. M. BJØRNEBOE, ESTHER FRANTZEN, H. POULSEN and KIRSTEIN ROSENDAL, Nord. med. **50**:1094 (Aug. 6) 1953.

The authors present a bacteriological study in 39 children with primary acute laryngitis. Laryngeal swabs were taken in the course of direct laryngoscopy. Pneumococci in 8 patients; Hemophilus influenzae, 20; γ-streptococci, 37; Staphylococcus aureus, 14, and Gram-negative diplecocci, 11 were among the organisms found.

WALLGREN, Stockholm.

Nervous Diseases

TRICEPS SURAE SYNDROME IN CEREBRAL PALSY. L. D. BAKER, A. M. A. Arch. Surg. **68**:216 (Feb.) 1954.

In the past decade the conservative management of cerebral palsy has been favored and the benefits of surgical intervention minimized. Baker recommends wider use of surgical corrective procedures. In certain patients with spasticity of the lower extremities and equinus deformity of the feet, recession of the heads of the gastrocnemius will permit dorsiflexion of the ankle and extension of the knee, with the ankle dorsiflexed. Furthermore, the foot clonus will be reduced. This procedure should be considered before lengthening of the Achilles tendon is attempted or a partial neurectomy of the triceps surae is done.

LIST, Grand Rapids, Mich. [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

STUDY OF THALAMIC AND CORTICAL RHYTHMS IN PETIT MAL. D. WILLIAMS, Brain **76**:50 (March) 1953.

Williams presents his fascinating work in which electroencephalographic records were obtained from the thalamus, white matter, and cerebral cortex during true petit mal seizures in children. Only six children with a large number of seizures were studied, as the prerequisites were sufficiently frequent petit mall attacks, typical rhythmic 3-per-second wave and spike discharges on EEG, and ventriculography, which was necessary for reasonably accurate placement of the coaxial electrodes.

The sequence of events in the petit mal attack was found to be as follows: A rhythm of 3 per second begins deep in the thalamus. It increases in voltage and persistence until it reaches the cortex, at which time a fast spike originates deep in the cortex. The "initial spike" usually has a high voltage and travels down to the thalamus, either directly or via more superficial layers of the cortex. As the spike reaches the thalamus, the site of origin of the 3-per-second wave alters and becomes more superficial (lateral and ventral) within the thalamus. The wave which arises in the new position in the thalamus is then followed by a spike arising from deep in the cortex, etc. As the attack proceeds, the rate usually slows to 2.5 per second, and the voltage of the cortical spike drops, then ceases. The wave then disappears. Although the thalamic rhythm seems to be responsible for the cortical spike, the latter seems to be essential for continuation of the 3-per-second rhythm; if the wave recommences and no spike occurs, the rhythm is not sustained. If the rhythm does not recur in a constant position deep in the thalamus, it does not develop a cortical spike, the rhythm dies, and the attack is aborted.

Williams advances the hypothesis that petit mal attacks are due to a disturbance in the thalamus which causes a rhythmic discharge throughout the cortex. Petit mal may be regarded as a periodic disorganization of the afferent, affector side of the organism, which inhibits all awareness and "spontaneous" behavior, in contrast to other forms of epilepsy, in which the disorganization may be considered to occur in the effector mechanisms.

It should be noted that this study is the first work of this nature in humans.

JOHNS, New York [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

MEGALENCEPHALY ASSOCIATED WITH HYALINE PAN-NEUROPATHY. L. CROME, Brain **76**:215 (June) 1953.

Crome records the case of a child in whom convulsions began at the age of 4 months, with enlargement of the head but no evidence of increased intracranial pressure, followed by mental retardation, generalized rigidity, and opisthotonos. The child died at 26 months of age. Pathologically, there was megalencephaly, localized dilatation of the lateral ventricles, spongy degeneration of the white matter, and loss of nerve cells and glial proliferation in the overlying cortex. Similar changes were found in the basal ganglia. Numerous hyaline bodies were found throughout the central nervous system and available proximal portions of the spinal and cranial nerves, being especially dense in the subpial zone of the cortex, brain stem, and spinal cord, around the blood vessels, and in the area of the subarcuate fibers of the centrum semiovale. These bodies stained similarly to fibrin and fibrinoid material, except that they were negative to periodic acid-Schiff stain and were only partially argyrophilic. It was suggested that the hyaline bodies were formed as a result of interaction between the formed tissue elements in the brain and nerves with the "ground substances" or with the derivatives of the cerebrospinal fluid or plasma. It was believed that the case fell into the group of secondary megalencephaly.

JOHNS, New York [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

TREATMENT OF BELL'S PALSY WITH CORTISONE. W. P. ROBISON and B. F. MOSS, J. A. M. A. **154**:142 (Jan. 9) 1954.

Most authorities feel that in patients suffering with severe Bell's palsy recovery is not likely to occur in less than several months. Robison and Moss treated two patients with cortisone, and prompt recovery occurred.

With one, a girl aged 13, treatment was started on the third day of paralysis. Three days after the cortisone therapy was begun the patient showed improvement that was obvious and gratifying. During this time 400 mg. of cortisone had been given. For the next 10 days 75 mg. of cortisone was given each day (a total dose of 1,150 mg.), with continuing improvement. Recovery was complete 19 days after onset.

Cortisone therapy was started one week after onset of the paralysis in the second patient, a child aged 5 years. Cortisone was given in diminishing doses, and recovery was complete on the 17th day.

According to Rothendler, "the beneficial action of cortisone in these patients can be assumed to be due to a reduction of congestion and related ischemia of the nerve and its sheath in the bony canal." The authors suggest the use of cortisone in the early stages of Bell's palsy.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

AN UNUSUAL CONGENITAL ANOMALY OF THE BRAIN: AGENESIS OF THE CORPUS CALLOSUM, ABSENCE OF THE SEPTUM PELLUCIDIUM, AND FUSION OF THE CEREBRAL HEMISPHERES. W. H. MOSBERG JR. and H. C. VORIS, J. Neuropath. & Exper. Neurol. **13**:369 (April) 1954.

The authors report on a boy who died at the age of 4½ years. It was noted that he was retarded at the age of 7 months, when he was unable to sit up alone. At the age of 3½ years he was unable to sit or walk without support and he could not talk. He appeared to be an alert child and was able to smile and to hold a spoon. The upper extremities showed athetoid movements. The muscle stretch reflexes were generally hypoactive, with bilateral sustained ankle clonus. The Babinski sign was absent. Autopsy revealed the brain to be fused anteriorly in one mass without disruption of the gyral pattern in the midline until 11 cm. posterior to the frontal poles. The gyral pattern was anomalous. Anteriorly there was a single midline ventricle, and the third ventricle appeared to be a continuation of the cavity. There was no evidence of lamina terminalis. There was no corpus callosum. The temporal horn was shortened. The internal capsule and the cerebral peduncles were rudimentary. There was no histologic evidence of Betz cells in the motor cortex. It appeared likely that development was arrested early in fetal life.

SIEKERT, Rochester, Minn. [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

Books

The Eczemas: A Symposium by Ten Authors. Edited by L. J. A. Loewenthal. Price, not given. Pp. 267, with 77 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1954.

This book, a collection of 13 short chapters, is an outstanding contribution. Probably the most important part is the 24-page article by H. Storck, of Zurich, on the role of bacteria in eczema. There is much evidence that in many of the cases of exudative eczema Staphylococcus aureus or a hemolytic Streptococcus is multiplying on the skin, that the reaction to this infection is an allergic one of the delayed reaction type, and that these bacteria may be responsible, at least in part, for resistance to treatment or spreading of the dermatitis. The newer antibiotics are useful; vaccines may be useful but must be used with caution.

Pediatricians will be especially interested in the chapter on atopic dermatitis, by Sulzberger and Witten. Although the infantile form is not covered as fully as one could wish, for a short chapter it is illuminating.

The chapter on the general principles of treatment, by Lowenthal, is a delight to read. Why do the great masters of dermatology get superior results? Just what is the proper place of cortisone in therapy today? How is psychotherapy to be used? These and many other questions are discussed with great clarity.

The above-mentioned articles are the ones that particularly appealed to this reviewer; others might prefer some of the following: "Contact Eczema: Some Clinical Considerations," by F. Ray Bettley, London; "Seborreic Dermatitis," by G. A. G. Peterkin, Edinburgh; "Allergic Eczema: Theoretical Considerations," by H. Haxthausen, Copenhagen; "Histopathology of Eczema," by Henry Haber, Prague; "Cutaneous Resistance to Alkalies, Acids, and Commercial Solvents," by W. Burckhardt, Zurich; "Eczematous Eruptions with Special Features," by S. Gordon, Johannesburg.

Finally, there is a chapter on treatment, with thirty-four prescriptions, by four of the above contributors. This book is a gold mine.

Hypertension and Nephritis. By Arthur M. Fishberg, M.D. Price, $12.50. Pp. 986, with 49 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1954.

The author has practically rewritten this well-known book to bring into it the new knowledge of the kidney and of hypertension acquired in the 15 years which have elapsed since the preceding edition was published. It has been necessary to increase the size of the book by over 200 pages to include these advances in knowledge. The physiology of the kidney in health and disease is well detailed. Renal function tests are discussed as to purpose, method of procedure, reliability, and clinical value. It is shown that a few simple and practical tests are adequate to determine quite accurately the kidney status at any time.

The subdivisions of Bright's disease are each described in considerable detail as to their etiology, pathogenesis, clinical course, and therapy. The difficulties in differential diagnosis, especially in the chronic forms of kidney disease, are cited, and suggestions are given to assist one in making an accurate determination of the underlying cause of the kidney ailment present. Diabetic glomerulosclerosis and chronic pyelonephritis are given special attention. Therapy in kidney disease is well detailed for all stages of the disease.

One-third of the book is devoted to the subject of essential hypertension. The etiology, pathogenesis, clinical course, and complications are given careful and thorough attention. Cushing's syndrome, pheochromocytoma, and the association of renal hypertensive disease in pregnancy are the subjects of special chapters.

The treatment of hypertension is accorded much consideration. The general management of the patient is strongly stressed. Pharmacological remedies are fairly presented in regard to their indications, possible benefits, undesirable side-effects, and observed limitations. Available surgical therapeutic procedures are outlined with their rationale, techniques, and immediate and remote results fully explained.

There are many subheadings in the table of contents which permit one to refer quickly to any desired information that is in the text. A very generous table of references is given at the end of each chapter, which can guide the reader directly to much of the literature available on hypertension and nephritis.

The Dynamics of Virus and Rickettsial Infections: International Symposium. Edited by Frank W. Hartman, Frank L. Horsfall Jr., and John G. Kidd. Price, not given. Pp. 461. Blakiston Company, 575 Madison Ave., New York 22, 1954.

This book presents the material from the 1953 "Detroit Symposium on Dynamics of Virus and Rickettsial Infections." The 33 papers have been divided into five sections, with the appropriate discussion included. The sections include mechanisms, ecology and pathogenesis, mechanics of immunity, laboratory diagnosis, and approaches to prophylaxis and therapy.

For the person interested in virus diseases and the recent developments in the fields of virus chemistry, mechanism of cell invasion, virus formation, and virus precursors, the first section is excellent. The articles are well written, and documented material from study of phage, plant, and animal viruses demonstrate the tremendous fundamental advances which have been made in the past few years.

The papers in the section on pathogenesis are also at a fundamental level and include plant and animal as well as human diseases. However, for the practitioner interested in a more precise understanding of clinical problems but not particularly interested in virology per se, papers on the "Pathogenic Mechanisms of Virus Diseases," by Hammon, and on "Variola," by Downie and McCarthy, are excellent. Most pediatricians should enjoy the entire section on immunity, since the general concepts of the epidemiologic picture as related to the immune states of populations and immunization with killed and attenuated viruses are discussed. The problem of poliomyelitis viruses is well covered.

In the laboratory section, there is much good general information on how to submit specimens and the difficulties of virus diagnosis in the laboratory. In addition, psittacosis lymphogranuloma infections and smallpox are well covered, as well as exciting new methods with tissue culture and other techniques.

In Section 5, the beginning of what promises to be specific chemothrapy for these infections is outlined. The only paper of immediate clinical value is on the treatment of rickettsial disease, which is good.

As indicated, this book is ideal for the person who would like to "catch up" with modern virology. The clinical material is subordinate to the over-all purpose of the book.

Rat Quality: A Consideration of Heredity, Diet and Disease. Proceedings of the Symposium held at Columbia University, College of Physicians and Surgeons, New York, New York, January 31, 1952. By W. E. Heston, G. E. Jay Jr., H. Kaunitz, H. P. Morris, J. B. Nelson, S. M. Poiley, C. A. Slanetz, Lois M. Zucker, and T. F. Zucker. Price, $2.50. Pp. 138. National Vitamin Foundation, Inc., 15 E. 58th St., New York 22, 1953.

As indicated by its title, this paper-bound volume constitutes the proceedings of a one-day symposium held at the School of Public Health of Columbia University on Jan. 31, 1952. The 32 participants included geneticists, nutritionists, veterinarians, and other biological research workers from universities (chiefly Columbia), research laboratories and hospitals, the National Institutes of Health, and pharmaceutical houses, as well as commercial animal breeders.

The symposium emphasized the fact that the experimental animal is the most complex and variable of all the laboratory "instruments" employed in biological research and that proper selection, feeding, and care are highly important to the outcome of any experiment. It points out that progress in improving and standardizing animals for experimental purposes is indicated by the organization of the Animal Care Panel, in Chicago, and the Institute of Animal Resources of the National Research Council. The papers and discussions of the symposium were concerned almost exclusively with the rat and included such subjects as growth criteria, respiratory and other diseases, inbred strains, breeding for certain qualities, genetic and nutrition factors which influence animal uniformity, and evaluation of commercial diets and semipurified stock diets. Members of the symposium hope to establish a register for rat stocks and strains similar to one for mice which has already proved its value, particularly in relation to cancer research.

The proceedings of this symposium on rat quality should be read by all research workers employing rats. Other biological and medical investigators will profit from the discussions of the relation of genetics, nutrition, general health, and environmental conditions to variability in the response of experimental subjects. Practicing physicians, particularly pediatricians, will find portions of the proceedings of value as background knowledge for clinical problems of human nutrition.

Diseases of the Liver. By Mitchell A. Spellberg, M.D. Price, $16.50. Pp. 646, with 93 illustrations. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1954.

There has long been a definite need for a treatise on liver disease written for the practitioner. The current books available dealing with this subject are either monograms on a particular phase of liver disease or "encyclopedias" consisting primarily of surveys of the old and recent literature. This latter type of book, while of inestimable value to the hepatologist, is of little use to the busy practitioner or the medical student who has neither the time nor the necessary background to evaluate or ferret out the pertinent data for his purpose. Dr. Spellberg has atempted to write a book from the "viewpoint of a clinician for clinicians" and has succeeded admirably in his goal.

The major emphasis throughout the book is on diagnosis and treatment. The author points out that the clinician has three approaches to study liver disease, all of which must be utilized and correctly interpreted in the intelligent recognition and treatment of hepatic disorders: the clinical, the anatomical, and the physiological approaches. All of the important liver function tests are described, and the author shows how they may be best applied to the individual problem.

The book is very complete and contains sections on the various dysfunctions of the liver, both the common and the rare, as well as chapters on the role of the liver in various extrahepatic diseases. Each of these discussions contains an excellent subsection on the differential diagnosis. There is no separate section on anatomy and physiology, but these topics are adequately presented throughout the book as they pertain to diagnosis and treatment.

The author has omitted the ancient and historical literature, except where it pertains to the current viewpoints. At the end of each subsection are brief summaries in bold type which will be of help to those wishing to find quickly the important information on any one subject.

The author has drawn heavily on his own clinical experience in formulating many of his viewpoints, and in this regard some may find minor points of difference. However, in general the discussions are excellent and the presentation sound. The bibliography is extensive, but the text is not adequately annotated and therefore is of limited value to those wishing to find exact references.

The illustrations are numerous and well reproduced. The type is clear, and the text is concise and easily read. The book is recommended both to medical students and to practitioners who wish an authoritative and clearly written text with the major emphasis on the clinical aspects of liver disease.

Aggression, Hostility, and Anxiety in Children. By Lauretta Bender, M.D. Price, $5.50. Pp. 184, with 13 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1954.

In this book, Dr. Bender gives a distillation of more than 20 years' experience with large numbers of disturbed children in the Children's Department of the Psychiatric Division of Bellevue Hospital. She gives summaries and examples of her group studies on 260 children and follow-up and reexaminations of 50 of these children. She also gives a thorough review of the literature on the subject of aggression, hostility, and anxiety in children. Her bibliography is very extensive, and anyone interested in this particular aspect of child behavior cannot afford to pass up this excellent study.

This book would be of small value to the pediatrician who has not had some training and experience with emotionally disturbed children. Since treatment of the problem is so specialized, one could put his time to more profitable use by reading texts and reports of a more general nature. Dr. Bender's work, especially in the first portions of her book, is overweighted with clinical reports.

As in her studies on phychotic children, she places great emphasis on organicity. There are many psychiatrists who disagree with her postulations, but from a pediatric point of view, many of these deserve serious consideration. One of the most constructive and valuable parts of this book is her chapter on the attitude of children toward death. She has dealt with this intricate, difficult, and emotionally laden subject with great dexterity and clarity.

There is a very interesting chapter on suicide in which she states that over a course of 14 years, when she observed a group of children who had expressed suicidal tendencies, none consumated their intentions. These children directed their aggressions against environment in asocial and delinquent behavior, or they submitted to the intolerable situations, suffering emotional and intellectual flattening and in many instances accepting refuge in institutions.

There is another chapter on homicidal aggression, and here, too, she emphasizes the organic factors, although she does deal rather extensively with dynamic factors.

There is an intensive presentation of fire-setting children, and she reports on her study of 60 children with a history of fire-setting who were on her ward at Bellevue Hospital. She gives many case reports of these children's fantasies about fire, which represent a strong force which can give them power over adults, partially magical in nature. She then sets forth nine characteristics of fire-setting children. And all of these had to do with poor adaptation by the child to his environment. The relationship between fire-setting and enuresis is dealt with in clear detail.

The unique characteristic of this book is derived from utilization of the data to evolve a concept and deviate personality development as a result of aggression, hostility, and anxiety.

Neurosurgery of Infancy and Childhood. By Franc D. Ingraham and Donald D. Matson. Price, $15.00. Pp. 456, with 378 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1954.

Seldom does it fall to the lot of the reviewer to read a book with which he is in wholehearted agreement, but in this case it is happily true. On the other hand, to disagree with those with such a vast experience would be foolhardy indeed. The Children's Medical Center in Boston is the place of origin of this work, and it represents the experiences there in diagnostic studies and the surgical care of patients on the neurological service. It is pointed out that the surgical physiology of the child is modified by the factor of growth, and in many instances what might be regarded as proper treatment for adults is often quite unsatisfactory in a child.

The entire field of pediatric neurosurgery is covered by dividing the book into 10 parts. The major parts are concerned with congenital anomalies, hydrocephalus, trauma, and tumors of the nervous system. The smaller parts are on infection, cerebrovascular disorders, epilepsy, lead encephalopathy, and pediatric neurosurgical anesthesia. The authors are careful to mention that this book is not intended as an encyclopedia but that it represnts their own way of dealing with various situations.

The fact that the material for the chapter on spina bifida and cranium bifidum is based on 1,433 cases indicates the experience which supports their views. It is interesting to note that in meningomyelocele operation is delayed from 3 to 12 months, provided the covering of the sac is sufficiently tough to allow for home care. Mothers are supervised and given specific instructions in the care of the child. It is considered unwise to excise the sac until hydrocephalus, when it is present, is either controlled by surgical means or undergoes spontaneous arrest. Encephalocele, on the other hand, is usually dealt with surgically in the early weeks of life. Hydrocephalus, in this clinic, is not regarded as a hopeless condition, and thanks to a great deal of original work, many successful results can be recorded. Here again there has been a large experience with the old methods and with those developed by them, principally shunt operations such as ureteroarachnoid shunts. The section on trauma is excellent. The difference between the treatment of subdural hematoma in infants and in adults is emphasized.

The chapters on tumors of the nervous system will be of particular interest to neurologists and neurosurgeons, for in these, the details of 313 consecutive intracranial and 63 spinal cord tumors are collected. Forty per cent of the intracranial neoplasms occurred above the tentorium, which is considerably higher than is usually suspected. The diagnosis of so many supratentorial tumors probably represents careful diagnostic work, for it is well known that the symptoms and signs in children are meager. Many of the subjective neurological examinations, such as visual fields and tests for memory and aphasia, cannot be carried out. The diagnosis of spinal cord tumors in children is notoriously difficult, both on account of the inadequacy of the history and because of absence of complaints of sensory disturbances. Motor weakness is usually noticed first, then perhaps bladder symptoms. These are often confused with poliomyelitis and behavior disturbances.

The remaining parts of the book fill in the gaps between the major subjects, making a complete coverage of all things that such a volume could be expected to contain. In addition there is a selected bibliography of over 200 references, which covers the important work in pediatric neurosurgery.

This is an excellent book in a rather limited field, and even in the preface it is hard to find to whom it is directed. Certainly, neurological surgeons should have it and probably all those dealing with organic neurology. Pediatricians will find it useful, if only for the chapters on trauma and the sections on diagnoses. The volume should find its way to the shelves of any library that

prides itself on its ability to provide material on important subjects. Physicians not primarily interested in pediatrics may well browse through it, noting some of the facts and the set-up of the book. It is clearly printed in large readable type; the tables and illustrations are excellent.

A Handbook on Diseases of Children. Edition 6. By Bruce Williamson, M.D., F.R.C.P. Price, $4.50. Pp. 476, with 98 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1953.

This book is a short compendium, or handbook, in the field of pediatrics. Although apparently meant for medical students, since constant reference is made to them throughout the text, it may be considered as a refresher for the practitioner as well because many entities are discussed in sentences or small paragraphs. This book stands out in contrast to American textbooks of pediatrics, the latter containing 1,200 to 1,500 pages and discussing individual entities much more completely than could be done in the 467 pages of this book. Thus it could, at best, be considered only as a rapid reference book on the diseases of children. The convenient subheadings lend it easily to quick reference and also facilitate immensely the use of the book for this function. There is no bibliography appended to references made to the work of others, which presents the author in an unusually authoritative light. Therapy and treatment of subjective symptoms are given much import, and many time-honored but quasiscientific treatments, such as gargles, paints, poultices, "alimentary correctives," and "antiacid aperients," are suggested; favorite "prescriptions" and "recipes" for much symptomatic therapy are recommended.

It is an interesting commentary that about one-eighth of the book is given over to detailed and academic discussion of disorders of the heart, which seems more than warranted in a text which is meant to be so relatively abbreviated. Despite the recent advent of interest in congenital heart anomalies, both in diagnosis and in the newer surgical corrections, only five pages is devoted to this newer phase of cardiology. Perhaps a provincial interest in acquired and organic heart disease, which appears to be more prevalent in England because of the recognized greater incidence of rheumatic fever, might perhaps account for the apparent imbalance in the treatment of the various pediatric entities.

An exception is taken to the statement by the author that, "The separation of diseases of children from general medicine in the curriculum (of the medical student) is most unfortunate." The current and basic teaching in this country has been pointedly to the contrary, that children are not miniature adults and that their responses to disease, as well as the effect of pathological processes upon them, are unique from those of the adult organism. Emphasis has always been placed on the differences of child physiology and pathology from the physiology and pathology of the adult, which idea seems to be diametrically opposed to the inference of the writer. This may be the personal opinion of the author of the text under discussion, rather than a universal opinion of the teachers of pediatrics in England.

The more liberal attitudes, as expressed by modern child culture in America, seem not to have permeated the strict British teaching on child rearing. Such statements as the following demonstrate this difference: "As soon as the breast milk is fully established, regular feeding habits must be insisted upon, and the infant should be awakened at the proper time. . . . the infant must become used to the spoon and the cup and should be weaned from the bottle completely by the ninth month." This philosophy was current in this country 30 years ago, but a general trend to less regimentation has taken place here because of the accepted needs of the young person and is scarcely debated at present.

There are many other differences noted in the section on infant feeding, as compared to the accepted modern American methods. Human milk is still analyzed as to protein and fat, but what conclusions are made is not stated. The custom of adding solid food supplements to the infant dietary regimen as early as the fourth week, as is routinely done here, apparently would not be considered, as stated by this text. Broth and egg yolk are given by the fourth month, but starches, vegetables, and fruit are withheld until about the ninth month. Many other differences in feeding are noted.

There is an excellent discussion and brief summary of the antibiotics and sulfonamide drugs, as well as of the newer hormone substances, such as corticotropin (ACTH) and cortisone. The book is well indexed by proper nouns and minor subjects. It would be an interesting handbook for reference, but would not measure up to the American standard as a textbook in pediatrics for medical students in this country.

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1. Nelson, W. E.: Nutritional Edema (Protein Deficiency, Hypoproteinemia, War Edema), in Nelson, W. E.: Textbook of Pediatrics, ed. 6, Philadelphia, W. B. Saunders Company, 1954, pp. 308-309.

2. Dodd, K., and Minot, A. S.: Edema in Infancy and Childhood as Expression of Chronic Dietary Insufficiency, J. Pediat. *8*:442 (Apr.) 1936; Occurrence of Moderately Reduced Serum Albumin in 500 Children in a Southern Clinic, ibid *8*:452 (Apr.) 1936.

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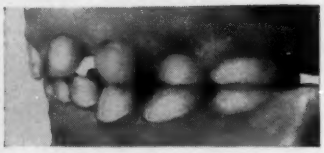

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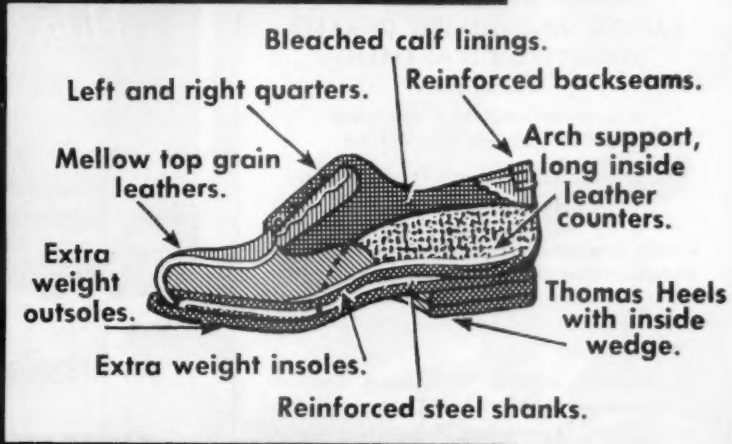

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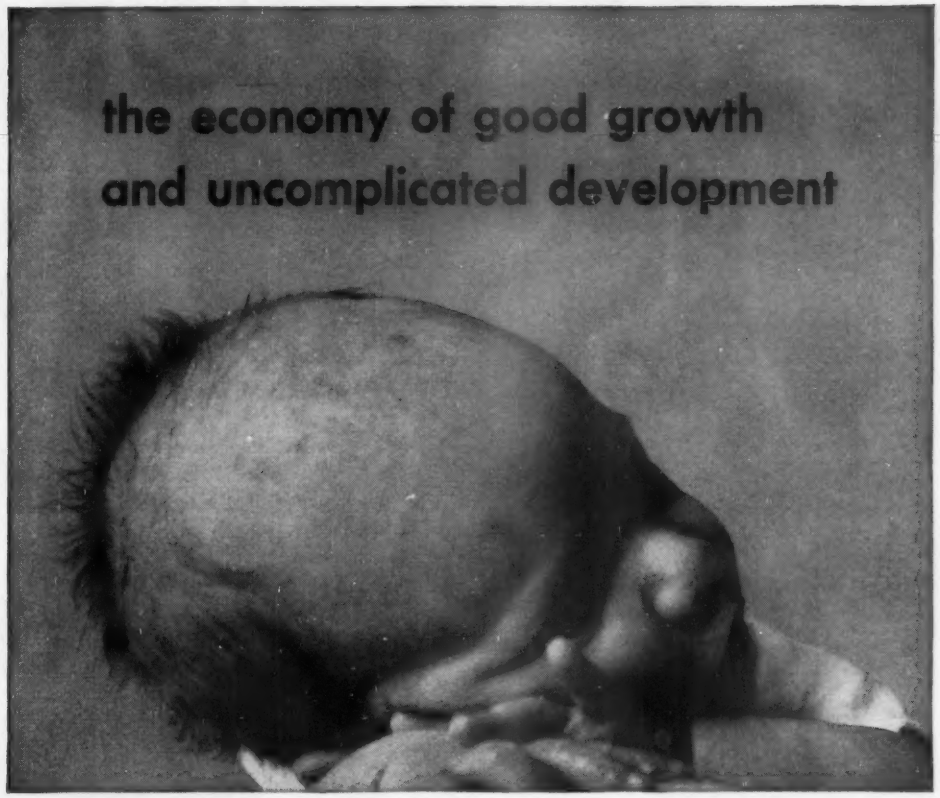

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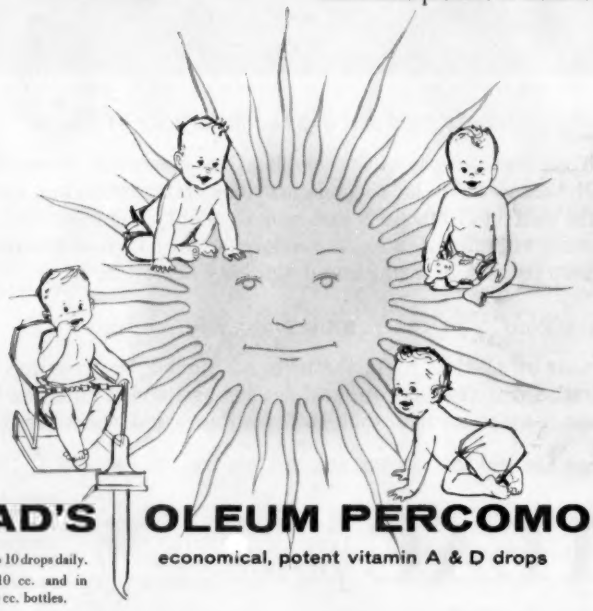

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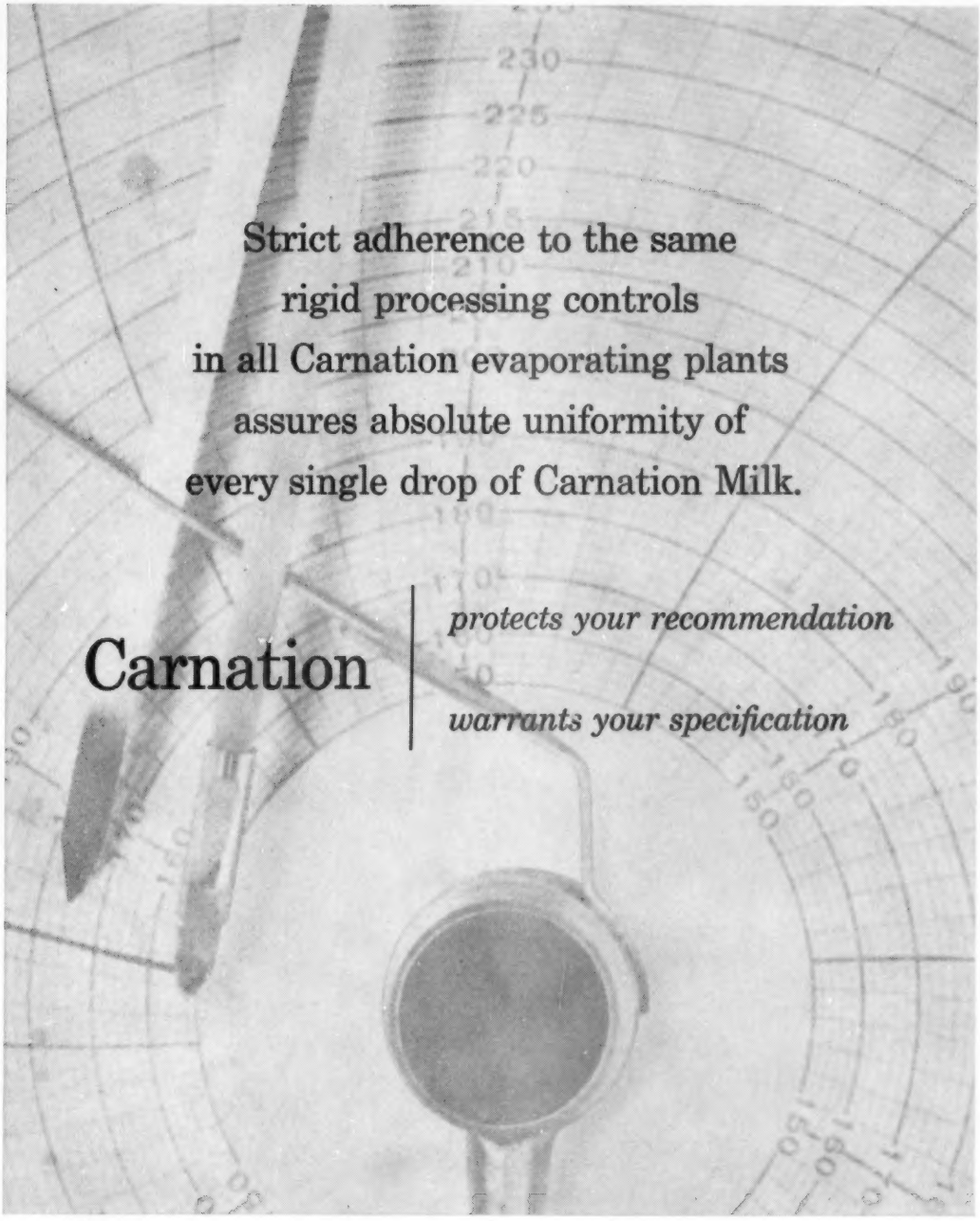

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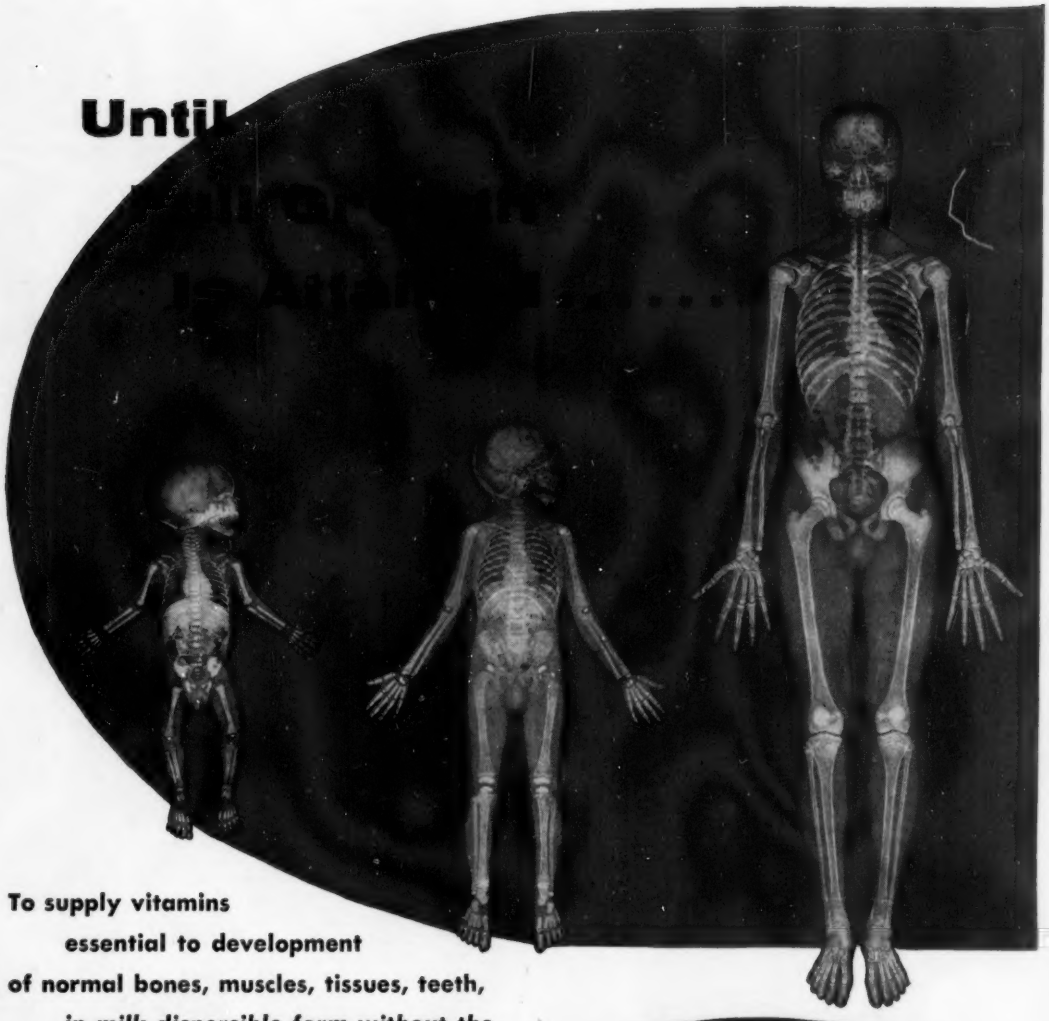

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